

**REMARKS**

It is respectfully requested that the above amendment be entered pursuant to the provisions of 37 C.F.R. §1.116(b); that this application be reconsidered in view of the above amendments and following remarks; and that all of the claims remaining in the application be allowed.

**THE CURRENT OFFICE ACTION UNDER REPLY:**

Claims 27-52 are currently pending. In the current Office Action, the Examiner has rejected the claims on the following grounds:

1. Under 35 U.S.C. §112, first paragraph, as allegedly lacking enabling disclosure in the specification as undue experimentation is required; and
2. Under 35 U.S.C. §112, second paragraph, as indefinite.

With the above amendments, Claim 27 has been amended and new Claims 53-56 have been added. Thus, Claims 27-56 are now pending. For the Examiner's convenience, the currently pending claims, as amended herein, are presented in Appendix B.

The rejections are addressed in part by the above amendments and in part by the arguments that follow.

**THE AMENDMENTS AND NEW CLAIMS:**

Claim 27 has been amended to delete the term "about."

Claims 48 and 50 have been amended to specify that the method is for treating a disease selected from the group consisting of asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, juvenile onset diabetes, inflammatory bowel disease, ulcerative colitis, Crohn's disease, multiple sclerosis, rheumatoid arthritis, tissue transplantation, tumor metastasis, meningitis, encephalitis, stroke, nephritis, retinitis, atopic dermatitis, psoriasis, myocardial ischemia, adult respiratory distress, erythema nodosum, allergic conjunctivitis, optic neuritis, uveitis, allergic rhinitis, Ankylosing spondylitis, psoriatic arthritis, vasculitis, Reiter's syndrome, systemic lupus erythematosus, progressive systemic sclerosis, polymyositis, dermatomyositis, Wegner's granulomatosis, aortitis, sarcoidosis,

lymphocytopenia, temporal arteritis, pericarditis, myocarditis, congestive heart failure, polyarteritis nodosa, hypersensitivity syndromes, allergy, hypereosinophilic syndromes, Churg-Strauss syndrome, chronic obstructive pulmonary disease, hypersensitivity pneumonitis, chronic active hepatitis, interstitial cystitis, autoimmune endocrine failure, primary biliary cirrhosis, autoimmune aplastic anemia, chronic persistent hepatitis, and thyroiditis. Support for this amendment is found on page lines 6 to 26 of the specification.

New independent Claim 53 has been added. The new claim incorporates the elements of previously pending Claims 27-33.

New dependent Claims 54-56 have also been added. These new claims are parallel in scope to Claims 48-52.

Applicants submit that these amendments place the claims in better condition for allowance or, alternatively, simplify issues for Appeal and, accordingly, entry of the amendment is earnestly solicited. Applicants reserve the right to pursue any canceled subject matter in a continuation or divisional case.

**THE REJECTION UNDER 35 U.S.C. §112, FIRST PARAGRAPH:**

The rejection under 35 U.S.C. §112, first paragraph, is based on the Examiner's assertion that it is unclear which compounds of Formula I have a binding affinity to VLA-4 of 15  $\mu$ m or less. The Examiner has based this assertion on the large number of compounds that are included within Formula 1 and has concluded that undue experimentation would be required for one of ordinary skill in the art to determine whether a compound of interest had a binding affinity to VLA-4 expressed by an  $IC_{50}$  of 15 $\mu$ M or less. Applicants respectfully disagree.

As discussed in section 2164.01 of the MPEP, the test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). In order to determine whether the level of experimentation is under, the Federal Circuit in *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) has provided a list of factors that are to be considered in making such a determination. These factors are

- (A) The breadth of the claims;
- (B) The nature of the invention;
- (C) The state of the prior art;
- (D) The level of one of ordinary skill;
- (E) The level of predictability in the art;
- (F) The amount of direction provided by the inventor;
- (G) The existence of working examples; and
- (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

As the Examiner will see, each of these factors clearly supports the fact that undue experimentation is not required to practice the present invention and that the present claims are fully enabled.

#### **Breadth of Claims**

While the Examiner has stated that Claim 27 represents a genus spanning millions of compounds, the Claim is specifically directed to those compounds that have a binding affinity to VLA-4 as expressed by an IC<sub>50</sub> of about 15  $\mu$ M or less. The actual number of compounds that fall within the scope of independent Claim 27 is irrelevant; the issue to be examined is whether the scope of the protection bears a reasonable relationship to the scope of enablement. *In re Fisher*, 472 F.2d 833, 166 USPQ 18 (CCPA 1970) and *In re Bowen*, 492 F.2d 859, 181 USPQ 48 (CCPA 1974). In this instance, several examples have been provided attesting to the range of compounds falling within the scope of the pending claims and providing a reasonable relationship between the breadth of the claims and the scope of enablement.

#### **Nature of Invention**

The nature of invention is inhibitors of leukocyte adhesion mediated by VLA-4.

### **State of the Prior Art**

Various methods of synthesizing the claimed Formula I compounds were known on the priority date of the present application, although, the compounds themselves and their ability to bind with VLA-4 was heretofore unknown. Additionally, methods for determining the binding affinity of compound for a specific sequence were also well known.

### **Level of Skill in the Art**

The level of skill in the relevant art is generally considered high, thereby tipping the balance toward the conclusion that a skilled artisan would be able to perform the claimed invention without undue experimentation.

### **Predictability**

In view of the disclosure of the specification, it is predictable that compounds having the structure of Formula I could easily be synthesized and that assays such as those disclosed in the Examples could be used determine whether such compounds have the requisite binding affinity for VLA-4.

### **Amount of Direction in the Specification**

As articulated above, the specification provides ample guidance as to how to make and use the claimed invention. The specification presents a detailed discussion of at least six different methods for synthesizing compounds of the present invention; see pages 61 to 83 of the specification as well as Method A-F and Examples 1-3.

With respect to methods for determining the bind affinity of the claimed compounds, the Examiner is directed to Examples A-C, which detail conventional assay methods that are suitable for use in practicing the present invention.

### **Number of Working Examples**

It is well established that specific examples are not required to meet the requirements of 35 U.S.C. §112, first paragraph. See *In re Strahilevitz*, 212 U.S.P.Q. 561, 563 (CCPA 1982); *Ex parte Nardi and Simier*, 229 U.S.P.Q. 79, 80 (BPAI 1986). In view of the large amount of knowledge in the prior art regarding VLA-4, assay techniques, and compound



synthesis, the guidance provided by the specification, the high predictability of the synthesis and assay techniques, and the high level of skill in the art, it is clear that the working examples provided in the application are more than sufficient.

#### **Amount of Experimentation Required**

Since methods of synthesizing compounds of Formula I and methods of determining the binding affinity of such compounds are known in the art or are provided by the specification, the amount of required experimentation is limited. The Examiner has apparently objected to the fact that it may be necessary for one of skill in the art to screen the compounds of Formula I to determine if they possess the requisite binding affinity. As discussed in *In re Wands*, "[e]nablement is not precluded by the necessity of some experimentation such as routine screening." In this instance, the screening of Formula I compounds to determine their binding affinity for VLA-4 is entirely a routine matter and in no way requires undue experimentation.

In conclusion, given that synthesis and assay methods for carrying out the claimed invention are well known in the art, no undue experimentation is required and independent Claim 27 is fully enabled by the specification. With respect to the new claims, as independent Claim 53 encompasses a subset of previously pending Claim 27, the above analysis is equally applicable and the new claims are also allowable. Reconsideration and withdrawal of the rejection are in order and are respectfully requested.

#### **THE REJECTIONS UNDER 35 U.S.C. §112, SECOND PARAGRAPH**

The rejections under 35 U.S.C. §112, second paragraph, are based on the following grounds:

1. As indefinite in that the metes and bounds of the term "about 15 $\mu$ M" are unclear;
2. As indefinite with respect to which diseases are mediated by VLA-4; and
3. As unclear with respect to the purpose of Claim 52.

Applicants submit that all of the pending claims satisfy the requirements of 35 U.S.C. §112, second paragraph, and traverse the rejection as follows.

**The Rejection as it Pertains to the Term "About":**

The Examiner has maintained his position that the term "about" is unclear. As discussed in the previous response, section 2173.05(b) of the MPEP clearly discusses the acceptability of the term. While continuing to disagree with the Examiner, in the interest of expediting prosecution, Applicants have amended Claim 27 to remove the objected to term. Reconsideration and withdrawal of the rejection is hereby requested.

**The Rejection as it Pertains to the Language Diseases Mediated by VLA-4:**

Claims 48 and 50 has been rejected by the Examiner as unclear with respect to the language "diseases mediated by VLA-4." In the previous response, Applicants direct the Examiner to the references discussing the various conditions associated with VLA-4 that have been incorporated by reference into the specification. While Applicants maintain that this rejection was made in error, in the interest of expediting prosecution, Claims 48 and 50 have been amended to recite specific VLA-4 mediated diseases. Reconsideration and withdrawal of the rejection are respectfully requested.

**The Rejection as it Pertains to the Purpose of Claim 52:**

The Examiner has asserted that Claim 52 is unclear as the Examiner is unable to determine just "what is to be accomplished." Claim 52 and new Claim 54 are directed to methods of binding VLA-4 in a biological sample. Applicants are uncertain as to what aspect of the claims' purpose the Examiner finds ambiguous. Applicants wish to point out that numerous patents that describe inhibitors of leukocyte adhesion mediated by VLA-4 have issued, the majority of which include claims directed to methods of binding. See Claim 19 of U.S. Patent No. 6,291,453, Claim 11 of U.S. Patent No. 6,362,341, Claim 28 of U.S. Patent No. 6,436,904, Claim 2 of U.S. Patent No. 6,465,513, Claim 22 of U.S. Patent No. 6,492,421, and Claim 18 of U.S. Patent No. 6,525,026.

While Applicants acknowledge that the Examiner is not bound by the actions of other Examiners in the U.S. Patent and Trademark Office, Applicants believe that consistent

treatment of similar claims and subject matter by the U.S. Patent and Trademark Office is generally desirable. Therefore, Applicants respectfully request that rejection be reconsidered and withdrawn or that the Examiner provide further detail regarding the exact basis for the rejection.


CONCLUSION

Accordingly, for the reasons set forth above, it is submitted that entry of this Amendment will place the application in condition for allowance and such entry and allowance are requested. Alternately, entry of this Amendment is requested as placing the application in better condition for appeal. A Notice of Appeal is being submitted herewith to prevent inadvertent abandonment of the application.

If the Examiner has any questions concerning this communication, please contact the undersigned at (650) 622-2300.

Respectfully submitted,

Date: May 23, 2003

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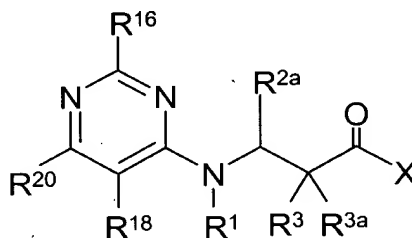
**APPENDIX A**

**REDACTED CLAIMS INDICATING AMENDMENTS MADE**

**In the Claims:**

Please amend claims 27, 48, and 50 and add new claims 53-56 as indicated below. Text to be deleted is indicated as ~~deleted text~~, while text to be added is underlined. For the Examiner's convenience, it is noted that the only amendment to claim 27 is the deletion of the term "about" from the last paragraph of claim 27.

27. (Amended) A compound of Formula (I):



(I)

wherein:

R<sup>1</sup> is selected from the group consisting of:

- A) hydrogen;
- B) alkyl of from 1 to 6 carbon atoms;
- C) substituted alkyl of from 1 to 10 carbon atoms, having 1 to 5 substituents selected from the group consisting of:
  - (1) alkoxy as defined in V herein;
  - (2) substituted alkoxy as defined in B<sup>1</sup> herein;
  - (3) acyl as defined in R<sup>1</sup> herein;
  - (4) acylamino as defined in S<sup>1</sup> herein;
  - (5) thiocarbonylamino as defined in B<sup>2</sup> herein;

- (6) acyloxy as defined in T<sup>1</sup> herein;
- (7) amino having the formula "-NH<sub>2</sub>-";
- (8) amidino having the formula "H<sub>2</sub>NC(=NH)-";
- (9) alkyl amidino wherein alkyl is defined in B herein and amidino is defined in C<sup>8</sup> herein;
- (10) thioamidino as defined in A<sup>2</sup> herein;
- (11) aminoacyl as defined in U<sup>1</sup> herein;
- (12) aminocarbonylamino as defined in V<sup>1</sup> herein;
- (13) aminothiocabonylamino as defined in W<sup>1</sup> herein;
- (14) aminocarbonyloxy as defined in X<sup>1</sup> herein;
- (15) aryl as defined in J herein;
- (16) substituted aryl as defined in K herein;
- (17) aryloxy as defined in I<sup>1</sup> herein;
- (18) substituted aryloxy as defined in J<sup>1</sup> herein;
- (19) aryloxyaryl having the formula "aryl-O-aryl";
- (20) substituted aryloxyaryl having the formula "aryl-O-aryl"  
substituted with from 1 to 3 substituents on either or both aryl  
rings selected from the group consisting of:
  - (a) hydroxy;
  - (b) acyl as defined in R<sup>1</sup> herein;
  - (c) acylamino as defined in S<sup>1</sup> herein;
  - (d) thiocarbonylamino as defined in B<sup>2</sup> herein;
  - (e) acyloxy as defined in T<sup>1</sup> herein;
  - (f) alkyl as defined in B herein;
  - (g) substituted alkyl as defined in C herein;
  - (h) alkoxy as defined in V herein;
  - (i) substituted alkoxy as defined in B<sup>1</sup> herein;
  - (j) alkenyl as defined in D herein;

- (k) substituted alkenyl as defined in E herein;
- (l) alkynyl as defined in U herein;
- (m) substituted alkynyl as defined in Q<sup>231</sup> herein;
- (n) amidino as defined in C8 herein;
- (o) alkylamidino wherein alkyl is defined in B herein and amidino is defined in C8 herein;
- (p) thioamidino as defined in A<sup>2</sup> herein;
- (q) amino as defined in C7 herein;
- (r) aminoacyl as defined in U<sup>1</sup> herein;
- (s) aminocarbonyloxy as defined in X<sup>1</sup> herein;
- (t) aminocarbonylamino as defined in V<sup>1</sup> herein;
- (u) aminothiocabonylamino as defined in W<sup>1</sup> herein;
- (v) aryl as defined in J herein;
- (w) substituted aryl as defined in K herein;
- (x) aryloxy as defined in I<sup>1</sup> herein;
- (y) substituted aryloxy as defined in J<sup>1</sup> herein;
- (z) cycloalkoxy as defined in E<sup>1</sup> herein;
- (a<sup>1</sup>) substituted cycloalkoxy as defined in F<sup>1</sup> herein;
- (b<sup>1</sup>) heteroaryloxy as defined in K<sup>1</sup> herein;
- (c<sup>1</sup>) substituted heteroaryloxy as defined in L<sup>1</sup> herein;
- (d<sup>1</sup>) heterocyclyloxy as defined in M<sup>1</sup> herein;
- (e<sup>1</sup>) substituted heterocyclyloxy as defined in N<sup>1</sup> herein;
- (f<sup>1</sup>) carboxyl;
- (g<sup>1</sup>) carboxylalkyl wherein alkyl is defined in B herein;
- (h<sup>1</sup>) carboxyl-substituted alkyl wherein substituted alkyl is defined in C herein;
- (i<sup>1</sup>) carboxyl-cycloalkyl wherein cycloalkyl is defined in F herein;

- (j<sup>1</sup>) carboxyl-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
- (k<sup>1</sup>) carboxylaryl wherein aryl is defined in J herein;
- (l<sup>1</sup>) carboxyl-substituted aryl wherein substituted aryl is defined in K herein;
- (m<sup>1</sup>) carboxylheteroaryl wherein heteroaryl is defined in L herein;
- (n<sup>1</sup>) carboxyl-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (o<sup>1</sup>) carboxylheterocyclic wherein heterocyclic is defined in N herein;
- (p<sup>1</sup>) carboxyl-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (q<sup>1</sup>) carboxylamido;
- (r<sup>1</sup>) cyano;
- (s<sup>1</sup>) thiol as defined in X<sup>2</sup> herein;
- (t<sup>1</sup>) thioalkyl as defined in X herein;
- (u<sup>1</sup>) substituted thioalkyl as defined in C42 herein;
- (v<sup>1</sup>) thioaryl as defined in C43 herein;
- (w<sup>1</sup>) substituted thioaryl as defined in C44 herein;
- (x<sup>1</sup>) thioheteroaryl as defined in C47 herein;
- (y<sup>1</sup>) substituted thioheteroaryl as defined in C48 herein;
- (z<sup>1</sup>) thiocycloalkyl as defined in C45 herein;
- (a<sup>2</sup>) substituted thiocycloalkyl as defined in C46 herein;
- (b<sup>2</sup>) thioheterocyclic as defined in C49 herein;
- (c<sup>2</sup>) substituted thioheterocyclic as defined in C50 herein;
- (d<sup>2</sup>) cycloalkyl as defined in F herein;
- (e<sup>2</sup>) substituted cycloalkyl as defined in G herein;

- (f<sup>2</sup>) guanidino as defined in C38 herein;
- (g<sup>2</sup>) guanidinosulfone as defined in C39 herein;
- (h<sup>2</sup>) halo as defined in Q herein;
- (i<sup>2</sup>) nitro;
- (j<sup>2</sup>) heteroaryl as defined in L herein;
- (k<sup>2</sup>) substituted heteroaryl as defined in M herein;
- (l<sup>2</sup>) heterocyclic as defined in N herein;
- (m<sup>2</sup>) substituted heterocyclic as defined in O herein;
- (n<sup>2</sup>) cycloalkoxy as defined in E<sup>1</sup> herein;
- (o<sup>2</sup>) substituted cycloalkoxy as defined in F<sup>1</sup> herein;
- (p<sup>2</sup>) heteroaryloxy as defined in K<sup>1</sup> herein;
- (q<sup>2</sup>) substituted heteroaryloxy as defined in L<sup>1</sup> herein;
- (r<sup>2</sup>) heterocyclyloxy as defined in M<sup>1</sup> herein;
- (s<sup>2</sup>) substituted heterocyclyloxy as defined in N<sup>1</sup> herein;
- (t<sup>2</sup>) oxycarbonylamino as defined in Y<sup>1</sup> herein;
- (u<sup>2</sup>) oxythiocarbonylamino as defined in Z<sup>1</sup> herein;
- (v<sup>2</sup>) -S(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (w<sup>2</sup>) -S(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (x<sup>2</sup>) -S(O)<sub>2</sub>-cycloalkyl wherein cycloalkyl is defined in F herein;
- (y<sup>2</sup>) -S(O)<sub>2</sub>-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
- (z<sup>2</sup>) -S(O)<sub>2</sub>-alkenyl wherein alkenyl is defined in D herein;
- (a<sup>3</sup>) -S(O)<sub>2</sub>-substituted alkenyl wherein substituted alkenyl is defined in E herein;
- (b<sup>3</sup>) -S(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;



- (c<sup>3</sup>) -S(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (d<sup>3</sup>) -S(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (e<sup>3</sup>) -S(O)<sub>2</sub>-substituted heteroaryl wherein substituted aryl is defined in M herein;
- (f<sup>3</sup>) -S(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (g<sup>3</sup>) -S(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (h<sup>3</sup>) -OS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (i<sup>3</sup>) -OS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (j<sup>3</sup>) -OS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (k<sup>3</sup>) -OS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (l<sup>3</sup>) -OS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (m<sup>3</sup>) -OS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (n<sup>3</sup>) -OS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (o<sup>3</sup>) -OS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (p<sup>3</sup>) -OSO<sub>2</sub>-NRR where R is:
  - (i) hydrogen; or
  - (ii) alkyl as defined in B herein;
- (q<sup>3</sup>) -NRS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;

- (r<sup>3</sup>) -NRS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (s<sup>3</sup>) -NRS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (t<sup>3</sup>) -NRS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (u<sup>3</sup>) -NRS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (v<sup>3</sup>) -NRS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (w<sup>3</sup>) -NRS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (x<sup>3</sup>) -NRS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (y<sup>3</sup>) -NRS(O)<sub>2</sub>-NR-alkyl wherein alkyl is defined in B herein;
- (z<sup>3</sup>) -NRS(O)<sub>2</sub>-NR-substituted alkyl wherein substituted alkyl is defined in C herein;
- (a<sup>4</sup>) -NRS(O)<sub>2</sub>-NR-aryl wherein aryl is defined in J herein;
- (b<sup>4</sup>) -NRS(O)<sub>2</sub>-NR-substituted aryl wherein substituted aryl is defined in K herein;
- (c<sup>4</sup>) -NRS(O)<sub>2</sub>-NR-heteroaryl wherein heteroaryl is defined in L herein;
- (d<sup>4</sup>) -NRS(O)<sub>2</sub>-NR-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (e<sup>4</sup>) -NRS(O)<sub>2</sub>-NR-heterocyclic wherein heterocyclic is defined in N herein;

- (f<sup>4</sup>) -NRS(O)<sub>2</sub>-NR-substituted heterocyclic wherein substituted heterocyclic is defined in O herein and where R is:
- (i) hydrogen; or
  - (ii) alkyl as defined in B herein;
- (g<sup>4</sup>) mono- and di-alkylamino wherein alkylamino is defined in I<sup>2</sup>9 herein;
- (h<sup>4</sup>) mono- and di-(substituted alkyl)amino wherein substituted alkylamino is defined in I<sup>2</sup>10 herein;
- (i<sup>4</sup>) mono- and di-arylamino wherein aryl is defined in J herein and amino is defined in C7 herein;
- (j<sup>4</sup>) mono- and di-substituted arylamino wherein substituted aryl is defined in K herein and amino is defined in C7 herein;
- (k<sup>4</sup>) mono- and di-heteroarylamino wherein heteroaryl is defined in L herein and amino is defined in C7 herein;
- (l<sup>4</sup>) mono- and di-substituted heteroarylamino wherein substituted heteroaryl is defined in M herein and amino is defined in C7 herein;
- (m<sup>4</sup>) mono- and di-heterocyclic amino wherein heterocyclic is defined in N herein and amino is defined in C7 herein;
- (n<sup>4</sup>) mono- and di-substituted heterocyclic amino wherein substituted heterocyclic is defined in O herein and amino is defined in C7 herein;
- (o<sup>4</sup>) unsymmetric di-substituted amines having different substituents selected from:
- (i) alkyl as defined in B herein;

- (ii) substituted alkyl as defined in C herein;
  - (iii) aryl as defined in J herein;
  - (iv) substituted aryl as defined in K herein;
  - (v) heteroaryl as defined in L herein;
  - (vi) substituted heteroaryl as defined in M herein;
  - (vii) heterocyclic as defined in N herein;
  - (viii) substituted heterocyclic as defined in O herein;
- and

(ix) amino groups, as defined in C7 herein, on the substituted aryl blocked by conventional blocking groups such as Boc, Cbz, formyl, and the like or substituted with -SO<sub>2</sub>NRR where R is:

- (a) hydrogen; or
- (b) alkyl as defined in B herein;

- (21) cyano;
- (22) halogen as defined in Q herein;
- (23) hydroxyl;
- (24) nitro;
- (25) carboxyl;
- (26) carboxylalkyl wherein alkyl is defined in B herein;
- (27) carboxyl-substituted alkyl wherein substituted alkyl is defined in C herein;
- (28) carboxyl-cycloalkyl wherein cycloalkyl is defined in F herein;
- (29) carboxyl-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
- (30) carboxylaryl wherein aryl is defined in J herein;
- (31) carboxyl-substituted aryl wherein substituted aryl is defined in K herein;

- (32) carboxylheteroaryl wherein heteroaryl is defined in L herein;
- (33) carboxyl-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (34) carboxylheterocyclic wherein heterocyclic is defined in N herein;
- (35) carboxyl-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (36) cycloalkyl as defined in F herein;
- (37) substituted cycloalkyl as defined in G herein;
- (38) guanidino having the formula -NRC(=NR)NRR, -NRC(=NR)NR-alkyl, -NRC(=NR)NR-substituted alkyl, -NRC(=NR)NR-alkenyl, -NRC(=NR)NR-substituted alkenyl, -NRC(=NR)NR-alkynyl, -NRC(=NR)NR-substituted alkynyl, -NRC(=NR)NR-aryl, -NRC(=NR)NR-substituted aryl, -NRC(=NR)NR-cycloalkyl, -NRC(=NR)NR-heteroaryl, -NRC(=NR)NR-substituted heteroaryl, -NRC(=NR)NR-heterocyclic, and -NRC(=NR)NR-substituted heterocyclic where each R is independently hydrogen and alkyl as well as where one of the amino groups is blocked by conventional blocking groups such as Boc, Cbz, formyl, and the like and wherein alkyl is defined in B herein; substituted alkyl is defined in C herein; alkenyl is defined in D herein; substituted alkenyl is defined in E herein; alkynyl is defined in U herein; substituted alkynyl is defined in Q<sup>231</sup> herein; cycloalkyl is defined in F herein; substituted cycloalkyl is defined in G herein; aryl is defined in J herein; substituted aryl is defined in K herein; heteroaryl is defined in L herein; substituted

- heteroaryl is defined in M herein; heterocyclic is defined in N herein; and substituted heterocyclic is defined in O herein;
- (39) guanidinosulfone having the formula  $\text{-NRC(=NR)NRSO}_2\text{-alkyl}$ ,  $\text{-NRC(=NR)NRSO}_2\text{-substituted alkyl}$ ,  $\text{-NRC(=NR)NRSO}_2\text{-alkenyl}$ ,  $\text{-NRC(=NR)NRSO}_2\text{-substituted alkenyl}$ ,  $\text{-NRC(=NR)NRSO}_2\text{-alkynyl}$ ,  $\text{-NRC(=NR)NRSO}_2\text{-substituted alkynyl}$ ,  $\text{-NRC(=NR)NRSO}_2\text{-aryl}$ ,  $\text{-NRC(=NR)NRSO}_2\text{-substituted aryl}$ ,  $\text{-NRC(=NR)NRSO}_2\text{-cycloalkyl}$ ,  $\text{-NRC(=NR)NRSO}_2\text{-substituted cycloalkyl}$ ,  $\text{-NRC(=NR)NRSO}_2\text{-heteroaryl}$ , and  $\text{-NRC(=NR)NRSO}_2\text{-substituted heteroaryl}$ ,  $\text{-NRC(=NR)NRSO}_2\text{-heterocyclic}$ , and  $\text{-NRC(=NR)NRSO}_2\text{-substituted heterocyclic}$  where each R is independently hydrogen and alkyl and wherein alkyl is defined in B herein; substituted alkyl is defined in C herein; alkenyl is defined in D herein; substituted alkenyl is defined in E herein; alkynyl is defined in U herein; substituted alkynyl is defined in Q<sup>231</sup> herein; cycloalkyl is defined in F herein; substituted cycloalkyl is defined in G herein; aryl is defined in J herein; substituted aryl is defined in K herein; heteroaryl is defined in L herein; substituted heteroaryl is defined in M herein; heterocyclic is defined in N herein; and substituted heterocyclic is defined in O herein;
- (40) thiol as defined in X<sup>2</sup> herein;
- (41) thioalkyl as defined in X herein;
- (42) substituted thioalkyl having the formula " $\text{-S-substituted alkyl}$ ";
- (43) thioaryl having the formula " $\text{-S-aryl}$ ";
- (44) substituted thioaryl having the formula " $\text{-S-substituted aryl}$ ";
- (45) thiocycloalkyl having the formula " $\text{-S-cycloalkyl}$ ";

- (46) substituted thiocycloalkyl having the formula "-S-substituted cycloalkyl";
- (47) thioheteroaryl having the formula "-S-heteroaryl";
- (48) substituted thioheteroaryl having the formula "-s-substituted heteroaryl";
- (49) thioheterocyclic having the formula "-S-heterocyclic";
- (50) substituted thioheterocyclic having the formula "-S-substituted heterocyclic";
- (51) heteroaryl as defined in L herein;
- (52) substituted heteroaryl as defined in M herein;
- (53) heterocyclic as defined in N herein;
- (54) substituted heterocyclic as defined in O herein;
- (55) cycloalkoxy as defined in E<sup>1</sup> herein;
- (56) substituted cycloalkoxy as defined in F<sup>1</sup> herein;
- (57) heteroaryloxy as defined in K<sup>1</sup> herein;
- (58) substituted heteroaryloxy as defined in L<sup>1</sup> herein;
- (59) heterocyclyloxy as defined in M<sup>1</sup> herein;
- (60) substituted heterocyclyloxy as defined in N<sup>1</sup> herein;
- (61) oxycarbonylamino as defined in Y<sup>1</sup> herein;
- (62) oxythiocarbonylamino as defined in Z<sup>1</sup> herein;
- (63) -OS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (64) -OS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (65) -OS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (66) -OS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (67) -OS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;

- (68) -OS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (69) -OS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (70) -OS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (71) -OSO<sub>2</sub>-NRR where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;
- (72) -NRS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (73) -NRS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (74) -NRS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (75) -NRS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (76) -NRS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (77) -NRS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (78) -NRS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (79) -NRS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (80) -NRS(O)<sub>2</sub>-NR-alkyl wherein alkyl is defined in B herein;
- (81) -NRS(O)<sub>2</sub>-NR-substituted alkyl wherein substituted alkyl is defined in C herein;
- (82) -NRS(O)<sub>2</sub>-NR-aryl wherein aryl is defined in J herein;
- (83) -NRS(O)<sub>2</sub>-NR-substituted aryl wherein substituted aryl is defined in K herein;



- (84) -NRS(O)<sub>2</sub>-NR-heteroaryl wherein heteroaryl is defined in L herein;
- (85) -NRS(O)<sub>2</sub>-NR-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (86) -NRS(O)<sub>2</sub>-NR-heterocyclic wherein heterocyclic is defined in N herein;
- (87) -NRS(O)<sub>2</sub>-NR-substituted heterocyclic wherein substituted heterocyclic is defined as O herein and where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;
- (88) mono- and di-alkylamino wherein alkylamino is defined in I<sup>29</sup> herein;
- (89) mono- and di-(substituted alkyl)amino wherein substituted alkylamino is defined in I<sup>210</sup> herein;
- (90) mono- and di-arylamino wherein aryl is defined in J herein and amino is defined in C7 herein;
- (91) mono- and di-substituted arylamino wherein substituted aryl is defined in K herein and amino is defined in C7 herein;
- (92) mono- and di-heteroarylamino wherein heteroaryl is defined in L herein and amino is defined in C7 herein;
- (93) mono- and di-substituted heteroarylamino wherein substituted heteroaryl is defined in M herein and amino is defined in C7 herein;
- (94) mono- and di-heterocyclic amino wherein heterocyclic is defined in N herein and amino is defined in C7 herein;
- (95) mono- and di-substituted heterocyclic amino wherein substituted heterocyclic is defined in O herein and amino is defined in C7 herein;

- (96) unsymmetric di-substituted amines having different substituents selected from:
- (a) alkyl as defined in B herein;
  - (b) substituted alkyl as defined in C herein;
  - (c) aryl as defined in J herein;
  - (d) substituted aryl as defined in K herein;
  - (e) heteroaryl as defined in L herein;
  - (f) substituted heteroaryl as defined in M herein;
  - (g) heterocyclic as defined in N herein;
  - (h) substituted heterocyclic as defined in O herein; and
  - (i) substituted alkyl groups having amino groups blocked by conventional blocking groups such as Boc, Cbz, formyl, and the like or alkyl/substituted alkyl groups substituted with:
    - (i) -SO<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
    - (ii) -SO<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
    - (iii) -SO<sub>2</sub>-alkenyl wherein alkenyl is defined in D herein;
    - (iv) -SO<sub>2</sub>-substituted alkenyl wherein substituted alkenyl is defined in E herein;
    - (v) -SO<sub>2</sub>-cycloalkyl wherein cycloalkyl is defined in F herein;
    - (vi) -SO<sub>2</sub>-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
    - (vii) -SO<sub>2</sub>-aryl wherein aryl is defined in J herein;
    - (viii) -SO<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;

- (ix) -SO<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
  - (x) -SO<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
  - (xi) -SO<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
  - (xii) -SO<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
  - and
  - (xiii) -SO<sub>2</sub>NRR where R is:
    - (a) hydrogen; or
    - (b) alkyl as defined in B herein;
- D) alkenyl of from 2 to 6 carbon atoms and from 1-2 sites of alkenyl unsaturation;
- E) substituted alkenyl of from 1 to 5 substituents selected from the group consisting of:
- (1) alkoxy as defined in V herein;
  - (2) substituted alkoxy as defined in B<sup>1</sup> herein;
  - (3) acyl as defined in R<sup>1</sup> herein;
  - (4) acylamino as defined in S<sup>1</sup> herein;
  - (5) thiocarbonylamino as defined in B<sup>2</sup> herein;
  - (6) acyloxy as defined in T<sup>1</sup> herein;
  - (7) amino as defined in C7 herein;
  - (8) amidino as defined in C8 herein;
  - (9) alkylamidino wherein alkyl is defined in B herein and amidino is defined in C8 herein;
  - (10) thioamidino as defined in A<sup>2</sup> herein;
  - (11) aminoacyl as defined in U<sup>1</sup> herein;

- (12) aminocarbonylamino as defined in V<sup>1</sup> herein;
- (13) aminothiocarbonylamino as defined in W<sup>1</sup> herein;
- (14) aminocarbonyloxy as defined in X<sup>1</sup> herein;
- (15) aryl as defined in J herein;
- (16) substituted aryl as defined in K herein;
- (17) aryloxy as defined in I<sup>1</sup> herein;
- (18) substituted aryloxy as defined in J<sup>1</sup> herein;
- (19) aryloxyaryl as defined in C19 herein;
- (20) substituted aryloxyaryl as defined in C20 herein;
- (21) halogen as defined in Q herein;
- (22) hydroxyl;
- (23) cyano;
- (24) nitro;
- (25) carboxyl;
- (26) carboxylalkyl wherein alkyl is defined in B herein;
- (27) carboxyl-substituted alkyl wherein substituted alkyl is defined in C herein;
- (28) carboxyl-cycloalkyl wherein cycloalkyl is defined in F herein;
- (29) carboxyl-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
- (30) carboxylaryl wherein aryl is defined in J herein;
- (31) carboxyl-substituted aryl wherein substituted aryl is defined in K herein;
- (32) carboxylheteroaryl wherein heteroaryl is defined in L herein;
- (33) carboxyl-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (34) carboxylheterocyclic wherein heterocyclic is defined in N herein;

- (35) carboxyl-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (36) cycloalkyl as defined in F herein;
- (37) substituted cycloalkyl as defined in G herein;
- (38) guanidino as defined in C38 herein;
- (39) guanidinosulfone as defined in C39 herein;
- (40) thiol as defined in X<sup>2</sup> herein;
- (41) thioalkyl as defined in X herein;
- (42) substituted thioalkyl as defined in C42 herein;
- (43) thioaryl as defined in C43 herein;
- (44) substituted thioaryl as defined in C44 herein;
- (45) thiocycloalkyl as defined in C45 herein;
- (46) substituted thiocycloalkyl as defined in C46 herein;
- (47) thioheteroaryl as defined in C47 herein;
- (48) substituted thioheteroaryl as defined in C48 herein;
- (49) thioheterocyclic as defined in C49 herein;
- (50) substituted thioheterocyclic as defined in C50 herein;
- (51) heteroaryl as defined in L herein;
- (52) substituted heteroaryl as defined in M herein;
- (53) heterocyclic as defined in N herein;
- (54) substituted heterocyclic as defined in O herein;
- (55) cycloalkoxy as defined in E<sup>1</sup> herein;
- (56) substituted cycloalkoxy as defined in F<sup>1</sup> herein;
- (57) heteroaryloxy as defined in K<sup>1</sup> herein;
- (58) substituted heteroaryloxy as defined in L<sup>1</sup> herein;
- (59) heterocyclyloxy as defined in M<sup>1</sup> herein;
- (60) substituted heterocyclyloxy as defined in N<sup>1</sup> herein;
- (61) oxycarbonylamino as defined in Y<sup>1</sup> herein;

- (62) oxythiocarbonylamino as defined in Z<sup>1</sup> herein;
- (63) -OS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (64) -OS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (65) -OS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (66) -OS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (67) -OS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (68) -OS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (69) -OS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (70) -OS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (71) OSO<sub>2</sub>-NRR where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;
- (72) -NRS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (73) -NRS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (74) -NRS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (75) -NRS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (76) -NRS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (77) -NRS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (78) -NRS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;

- (79) -NRS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (80) -NRS(O)<sub>2</sub>-NR-alkyl wherein alkyl is defined in B herein;
- (81) -NRS(O)<sub>2</sub>-NR-substituted alkyl wherein substituted alkyl is defined in C herein;
- (82) -NRS(O)<sub>2</sub>-NR-aryl wherein aryl is defined in J herein;
- (83) -NRS(O)<sub>2</sub>-NR-substituted aryl wherein substituted aryl is defined in K herein;
- (84) -NRS(O)<sub>2</sub>-NR-heteroaryl wherein heteroaryl is defined in L herein;
- (85) -NRS(O)<sub>2</sub>-NR-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (86) -NRS(O)<sub>2</sub>-NR-heterocyclic wherein heterocyclic is defined in N herein;
- (87) -NRS(O)<sub>2</sub>-NR-substituted heterocyclic wherein substituted heterocyclic is defined in O herein and where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;
- (88) mono- and di-alkylamino wherein alkylamino is defined in I<sup>29</sup> herein;
- (89) mono- and di-(substituted alkyl)amino wherein substituted alkylamino is defined in I<sup>210</sup> herein;
- (90) mono- and di-arylamino wherein aryl is defined in J herein and amino is defined in C7 herein;
- (91) mono- and di-substituted arylamino wherein substituted aryl is defined in K herein and amino is defined in C7 herein;
- (92) mono- and di-heteroarylamino wherein heteroaryl is defined in L herein and amino is defined in C7 herein;

- (93) mono- and di-substituted heteroaryl-amino wherein substituted heteroaryl is defined in M herein and amino is defined in C7 herein;
- (94) mono- and di-heterocyclic amino wherein heterocyclic is defined in N herein and amino is defined in C7 herein;
- (95) mono- and di-substituted heterocyclic amino wherein substituted heterocyclic is defined in O herein and amino is defined in C7 herein;
- (96) unsymmetric di-substituted amines having different substituents selected from:
  - (a) alkyl as defined in B herein;
  - (b) substituted alkyl as defined in C herein;
  - (c) aryl as defined in J herein;
  - (d) substituted aryl as defined in K herein;
  - (e) heteroaryl as defined in L herein;
  - (f) substituted heteroaryl as defined in M herein;
  - (g) heterocyclic as defined in N herein;
  - (h) substituted heterocyclic as defined in O herein; and
  - (i) substituted alkenyl groups having amino groups blocked by conventional blocking groups such as Boc, Cbz, formyl, and the like or alkenyl/substituted alkenyl groups substituted with:
    - (i) -SO<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
    - (ii) -SO<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
    - (iii) -SO<sub>2</sub>-alkenyl wherein alkenyl is defined in D herein;



- (iv) -SO<sub>2</sub>-substituted alkenyl wherein substituted alkenyl is defined in E herein;
  - (v) -SO<sub>2</sub>-cycloalkyl wherein cycloalkyl is defined in F herein;
  - (vi) -SO<sub>2</sub>-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
  - (vii) -SO<sub>2</sub>-aryl wherein aryl is defined in J herein;
  - (viii) -SO<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
  - (ix) -SO<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
  - (x) -SO<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
  - (xi) -SO<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
  - (xii) -SO<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein; and
  - (xiii) -SO<sub>2</sub>NRR where R is:
    - (a) hydrogen; or
    - (b) alkyl as defined in B herein;
- F) cycloalkyl of from 3 to 8 carbon atoms;
- G) substituted cycloalkyl of from 3 to 8 carbon atoms, having from 1 to 5 substituents selected from the group consisting of:
- (1) oxo (=O);
  - (2) thioxo (=S);
  - (3) alkoxy as defined in V herein;

- (4) substituted alkoxy as defined in B<sup>1</sup> herein;
- (5) acyl as defined in R<sup>1</sup> herein;
- (6) acylamino as defined in S<sup>1</sup> herein;
- (7) thiocarbonylamino as defined in B<sup>2</sup> herein;
- (8) acyloxy as defined in T<sup>1</sup> herein;
- (9) amino as defined in C7 herein;
- (10) amidino as defined in C8 herein;
- (11) alkylamidino wherein alkyl is defined in B herein and amidino is defined in C8 herein;
- (12) thioamidino as defined in A<sup>2</sup> herein;
- (13) aminoacyl as defined in U<sup>1</sup> herein;
- (14) aminocarbonylamino as defined in V<sup>1</sup> herein;
- (15) aminothiocarbonylamino as defined in W<sup>1</sup> herein;
- (16) aminocarbonyloxy as defined in X<sup>1</sup> herein;
- (17) aryl as defined in J herein;
- (18) substituted aryl as defined in K herein;
- (19) aryloxy as defined in I<sup>1</sup> herein;
- (20) substituted aryloxy as defined in J<sup>1</sup> herein;
- (21) aryloxyaryl as defined in C19 herein;
- (22) substituted aryloxyaryl as defined in C20 herein;
- (23) halogen as defined in Q herein;
- (24) hydroxyl;
- (25) cyano;
- (26) nitro;
- (27) carboxyl;
- (28) carboxylalkyl wherein alkyl is defined in B herein;
- (29) carboxyl-substituted alkyl wherein substituted alkyl is defined in C herein;

- (30) carboxyl-cycloalkyl wherein cycloalkyl is defined in F herein;
- (31) carboxyl-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
- (32) carboxylaryl wherein aryl is defined in J herein;
- (33) carboxyl-substituted aryl wherein substituted aryl is defined in K herein;
- (34) carboxylheteroaryl wherein heteroaryl is defined in L herein;
- (35) carboxyl-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (36) carboxylheterocyclic wherein heterocyclic is defined in N herein;
- (37) carboxyl-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (38) cycloalkyl as defined in F herein;
- (39) substituted cycloalkyl as defined in G herein;
- (40) guanidino as defined in C38 herein;
- (41) guanidinosulfone as defined in C39 herein;
- (42) thiol as defined in X<sup>2</sup> herein;
- (43) thioalkyl as defined in X herein;
- (44) substituted thioalkyl as defined in C42 herein;
- (45) thioaryl as defined in C43 herein;
- (46) substituted thioaryl as defined in C44 herein;
- (47) thiocycloalkyl as defined in C45 herein;
- (48) substituted thiocycloalkyl as defined in C46 herein;
- (49) thioheteroaryl as defined in C47 herein;
- (50) substituted thioheteroaryl as defined in C48 herein;
- (51) thioheterocyclic as defined in C49 herein;
- (52) substituted thioheterocyclic as defined in C50 herein;
- (53) heteroaryl as defined in L herein;

- (54) substituted heteroaryl as defined in M herein;
- (55) heterocyclic as defined in N herein;
- (56) substituted heterocyclic as defined in O herein;
- (57) cycloalkoxy as defined in E<sup>1</sup> herein;
- (58) substituted cycloalkoxy as defined in F<sup>1</sup> herein;
- (59) heteroaryloxy as defined in K<sup>1</sup> herein;
- (60) substituted heteroaryloxy as defined in L<sup>1</sup> herein;
- (61) heterocyclyloxy as defined in M<sup>1</sup> herein;
- (62) substituted heterocyclyloxy as defined in N<sup>1</sup> herein;
- (63) oxycarbonylamino as defined in Y<sup>1</sup> herein;
- (64) oxythiocarbonylamino as defined in Z<sup>1</sup> herein;
- (65) -OS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (66) -OS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (67) -OS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (68) -OS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (69) -OS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (70) -OS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (71) -OS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (72) -OS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (73) -OSO<sub>2</sub>-NRR where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;
- (74) -NRS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;

- (75) -NRS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (76) -NRS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (77) -NRS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (78) -NRS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (79) -NRS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (80) -NRS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (81) -NRS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (82) -NRS(O)<sub>2</sub>-NR-alkyl wherein alkyl is defined in B herein;
- (83) -NRS(O)<sub>2</sub>-NR-substituted alkyl wherein substituted alkyl is defined in C herein;
- (84) -NRS(O)<sub>2</sub>-NR-aryl wherein aryl is defined in J herein;
- (85) -NRS(O)<sub>2</sub>-NR-substituted aryl wherein substituted aryl is defined in K herein;
- (86) -NRS(O)<sub>2</sub>-NR-heteroaryl wherein heteroaryl is defined in L herein;
- (87) -NRS(O)<sub>2</sub>-NR-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (88) -NRS(O)<sub>2</sub>-NR-heterocyclic wherein heterocyclic is defined in N herein;
- (89) -NRS(O)<sub>2</sub>-NR-substituted heterocyclic wherein substituted heterocyclic is defined in O herein and where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;

- (90) mono- and di-alkylamino wherein alkylamino is defined in I<sup>2</sup>9 herein;
- (91) mono- and di-(substituted alkyl)amino wherein substituted alkylamino is defined in I<sup>2</sup>10 herein;
- (92) mono- and di-arylamino wherein aryl is defined in J herein and amino is defined in C7 herein;
- (93) mono- and di-substituted arylamino wherein substituted aryl is defined in K herein and amino is defined in C7 herein;
- (94) mono- and di-heteroarylamino wherein heteroaryl is defined in L herein and amino is defined in C7 herein;
- (95) mono- and di-substituted heteroarylamino wherein substituted heteroaryl is defined in M herein and amino is defined in C7 herein;
- (96) mono- and di-heterocyclic amino wherein heterocyclic is defined in N herein and amino is defined in C7 herein;
- (97) mono- and di-substituted heterocyclic amino wherein substituted heterocyclic is defined in O herein and amino is defined in C7 herein;
- (98) unsymmetric di-substituted amines having different substituents selected from:
  - (a) alkyl as defined in B herein;
  - (b) substituted alkyl as defined in C herein;
  - (c) aryl as defined in J herein;
  - (d) substituted aryl as defined in K herein;
  - (e) heteroaryl as defined in L herein;
  - (f) substituted heteroaryl as defined in M herein;
  - (g) heterocyclic as defined in N herein;
  - (h) substituted heterocyclic as defined in O herein; and

- (i) substituted alkynyl groups having amino groups blocked by conventional blocking groups such as Boc, Cbz, formyl, and the like or alkynyl/substituted alkynyl groups substituted with:
  - (i) -SO<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
  - (ii) -SO<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
  - (iii) -SO<sub>2</sub>-alkenyl wherein alkenyl is defined in D herein;
  - (iv) -SO<sub>2</sub>-substituted alkenyl wherein substituted alkenyl is defined in E herein;
  - (v) -SO<sub>2</sub>-cycloalkyl wherein cycloalkyl is defined in F herein;
  - (vi) -SO<sub>2</sub>-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
  - (vii) -SO<sub>2</sub>-aryl wherein aryl is defined in J herein;
  - (viii) -SO<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
  - (ix) -SO<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
  - (x) -SO<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
  - (xi) -SO<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
  - (xii) -SO<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein; and

- (xiii) -SO<sub>2</sub>NRR where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;
- H) cycloalkenyl of from 3 to 8 carbon atoms;
- I) substituted cycloalkenyl of from 3 to 8 carbon atoms, having from 1 to 5 substituents selected from the group consisting of:
  - (1) oxo (=O);
  - (2) thioxo (=S);
  - (3) alkoxy as defined in V herein;
  - (4) substituted alkoxy as defined in B<sup>1</sup> herein;
  - (5) acyl as defined in R<sup>1</sup> herein;
  - (6) acylamino as defined in S<sup>1</sup> herein;
  - (7) thiocarbonylamino as defined in B<sup>2</sup> herein;
  - (8) acyloxy as defined in T<sup>1</sup> herein;
  - (9) amino as defined in C7 herein;
  - (10) amidino as defined in C8 herein;
  - (11) alkylamidino wherein alkyl is defined in B herein and amidino is defined in C8 herein;
  - (12) thioamidino as defined in A<sup>2</sup> herein;
  - (13) aminoacyl as defined in U<sup>1</sup> herein;
  - (14) aminocarbonylamino as defined in V<sup>1</sup> herein;
  - (15) aminothiocarbonylamino as defined in W<sup>1</sup> herein;
  - (16) aminocarbonyloxy as defined in X<sup>1</sup> herein;
  - (17) aryl as defined in J herein;
  - (18) substituted aryl as defined in K herein;
  - (19) aryloxy as defined in I<sup>1</sup> herein;
  - (20) substituted aryloxy as defined in J<sup>1</sup> herein;
  - (21) aryloxyaryl as defined in C19 herein;



- (22) substituted aryloxyaryl as defined in C20 herein;
- (23) halogen as defined in Q herein;
- (24) hydroxyl;
- (25) cyano;
- (26) nitro;
- (27) carboxyl;
- (28) carboxylalkyl wherein alkyl is defined in B herein;
- (29) carboxyl-substituted alkyl wherein substituted alkyl is defined in C herein;
- (30) carboxyl-cycloalkyl wherein cycloalkyl is defined in F herein;
- (31) carboxyl-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
- (32) carboxylaryl wherein aryl is defined in J herein;
- (33) carboxyl-substituted aryl wherein substituted aryl is defined in K herein;
- (34) carboxylheteroaryl wherein heteroaryl is defined in L herein;
- (35) carboxyl-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (36) carboxylheterocyclic wherein heterocyclic is defined in N herein;
- (37) carboxyl-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (38) cycloalkyl as defined in F herein;
- (39) substituted cycloalkyl as defined in G herein;
- (40) guanidino as defined in C38 herein;
- (41) guanidiniosulfone as defined in C39 herein;
- (42) thiol as defined in X<sup>2</sup> herein;
- (43) thioalkyl as defined in X herein;
- (44) substituted thioalkyl as defined in C42 herein;

- (45) thioaryl as defined in C43 herein;
- (46) substituted thioaryl as defined in C44 herein;
- (47) thiocycloalkyl as defined in C45 herein;
- (48) substituted thiocycloalkyl as defined in C46 herein;
- (49) thioheteroaryl as defined in C47 herein;
- (50) substituted thioheteroaryl as defined in C48 herein;
- (51) thioheterocyclic as defined in C49 herein;
- (52) substituted thioheterocyclic as defined in C50 herein;
- (53) heteroaryl as defined in L herein;
- (54) substituted heteroaryl as defined in M herein;
- (55) heterocyclic as defined in N herein;
- (56) substituted heterocyclic as defined in O herein;
- (57) cycloalkoxy as defined in E<sup>1</sup> herein;
- (58) substituted cycloalkoxy as defined in F<sup>1</sup> herein;
- (59) heteroaryloxy as defined in K<sup>1</sup> herein;
- (60) substituted heteroaryloxy as defined in L<sup>1</sup> herein;
- (61) heterocyclyloxy as defined in M<sup>1</sup> herein;
- (62) substituted heterocyclyloxy as defined in N<sup>1</sup> herein;
- (63) oxycarbonylamino as defined in Y<sup>1</sup> herein;
- (64) oxythiocarbonylamino as defined in Z<sup>1</sup> herein;
- (65) -OS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (66) -OS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (67) -OS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (68) -OS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (69) -OS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;

- (70)  $-\text{OS}(\text{O})_2$ -substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (71)  $-\text{OS}(\text{O})_2$ -heterocyclic wherein heterocyclic is defined in N herein;
- (72)  $-\text{OS}(\text{O})_2$ -substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (73)  $-\text{OSO}_2$ -NRR where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;
- (74)  $-\text{NRS}(\text{O})_2$ -alkyl wherein alkyl is defined in B herein;
- (75)  $-\text{NRS}(\text{O})_2$ -substituted alkyl wherein substituted alkyl is defined in C herein;
- (76)  $-\text{NRS}(\text{O})_2$ -aryl wherein aryl is defined in J herein;
- (77)  $-\text{NRS}(\text{O})_2$ -substituted aryl wherein substituted aryl is defined in K herein;
- (78)  $-\text{NRS}(\text{O})_2$ -heteroaryl wherein heteroaryl is defined in L herein;
- (79)  $-\text{NRS}(\text{O})_2$ -substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (80)  $-\text{NRS}(\text{O})_2$ -heterocyclic wherein heterocyclic is defined in N herein;
- (81)  $-\text{NRS}(\text{O})_2$ -substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (82)  $-\text{NRS}(\text{O})_2$ -NR-alkyl wherein alkyl is defined in B herein;
- (83)  $-\text{NRS}(\text{O})_2$ -NR-substituted alkyl wherein substituted alkyl is defined in C herein;
- (84)  $-\text{NRS}(\text{O})_2$ -NR-aryl wherein aryl is defined in J herein;
- (85)  $-\text{NRS}(\text{O})_2$ -NR-substituted aryl wherein substituted aryl is defined in K herein;

- (86) -NRS(O)<sub>2</sub>-NR-heteroaryl wherein heteroaryl is defined in L herein;
- (87) -NRS(O)<sub>2</sub>-NR-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (88) -NRS(O)<sub>2</sub>-NR-heterocyclic wherein heterocyclic is defined in N herein;
- (89) -NRS(O)<sub>2</sub>-NR-substituted heterocyclic wherein substituted heterocyclic is defined in O herein and where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;
- (90) mono- and di-alkylamino wherein alkylamino is defined in I<sup>29</sup> herein;
- (91) mono- and di-(substituted alkyl)amino wherein substituted alkylamino is defined in I<sup>210</sup> herein;
- (92) mono- and di-arylamino wherein aryl is defined in J herein and amino is defined in C7 herein;
- (93) mono- and di-substituted arylamino wherein substituted aryl is defined in K herein and amino is defined in C7 herein;
- (94) mono- and di-heteroarylamino wherein heteroaryl is defined in L herein and amino is defined in C7 herein;
- (95) mono- and di-substituted heteroarylamino wherein substituted heteroaryl is defined in M herein and amino is defined in C7 herein;
- (96) mono- and di-heterocyclic amino wherein heterocyclic is defined in N herein and amino is defined in C7 herein;
- (97) mono- and di-substituted heterocyclic amino wherein substituted heterocyclic is defined in O herein and amino is defined in C7 herein;

(98) unsymmetric di-substituted amines having different substituents selected from:

- (a) alkyl as defined in B herein;
- (b) substituted alkyl as defined in C herein;
- (c) aryl as defined in J herein;
- (d) substituted aryl as defined in K herein;
- (e) heteroaryl as defined in L herein;
- (f) substituted heteroaryl as defined in M herein;
- (g) heterocyclic as defined in N herein;
- (h) substituted heterocyclic as defined in O herein; and
- (i) substituted alkynyl groups having amino groups blocked by conventional blocking groups such as Boc, Cbz, formyl, and the like or alkynyl/substituted alkynyl groups substituted with:
  - (i) -SO<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
  - (ii) -SO<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
  - (iii) -SO<sub>2</sub>-alkenyl wherein alkenyl is defined in D herein;
  - (iv) -SO<sub>2</sub>-substituted alkenyl wherein substituted alkenyl is defined in E herein;
  - (v) -SO<sub>2</sub>-cycloalkyl wherein cycloalkyl is defined in F herein;
  - (vi) -SO<sub>2</sub>-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
  - (vii) -SO<sub>2</sub>-aryl wherein aryl is defined in J herein;

- (viii) -SO<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (ix) -SO<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (x) -SO<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (xi) -SO<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (xii) -SO<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein; and
- (xiii) -SO<sub>2</sub>NRR where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;
- (J) aryl is an unsaturated aromatic carbocyclic group of from 6 to 14 carbon atoms;
- (K) substituted aryl of from 1 to 3 substituents selected from the group consisting of:
  - (1) hydroxy;
  - (2) acyl as defined in R<sup>1</sup> herein;
  - (3) acylamino as defined in S<sup>1</sup> herein;
  - (4) thiocarbonylamino as defined in B<sup>2</sup> herein;
  - (5) acyloxy as defined in T<sup>1</sup> herein;
  - (6) alkyl as defined in B herein;
  - (7) substituted alkyl as defined in C herein;
  - (8) alkoxy as defined in V herein;
  - (9) substituted alkoxy as defined in B<sup>1</sup> herein;
  - (10) alkenyl as defined in D herein;

- (11) substituted alkenyl as defined in E herein;
- (12) alkynyl as defined in U herein;
- (13) substituted alkynyl as defined in Q<sup>231</sup> herein;
- (14) amidino as defined in C8 herein;
- (15) alkylamidino wherein alkyl is defined in B herein and amidino is defined in C8 herein;
- (16) thioamidino as defined in A<sup>2</sup> herein;
- (17) amino as defined in C7 herein;
- (18) aminoacyl as defined in U<sup>1</sup> herein;
- (19) aminocarbonyloxy as defined in X<sup>1</sup> herein;
- (20) aminocarbonylamino as defined in V<sup>1</sup> herein;
- (21) aminothiocabonylamino as defined in W<sup>1</sup> herein;
- (22) aryl as defined in J herein;
- (23) substituted aryl as defined in K herein;
- (24) aryloxy as defined in I<sup>1</sup> herein;
- (25) substituted aryloxy as defined in J<sup>1</sup> herein;
- (26) cycloalkoxy as defined in E<sup>1</sup> herein;
- (27) substituted cycloalkoxy as defined in F<sup>1</sup> herein;
- (28) heteroaryloxy as defined in K<sup>1</sup> herein;
- (29) substituted heteroaryloxy as defined in L<sup>1</sup> herein;
- (30) heterocyclyloxy as defined in M<sup>1</sup> herein;
- (31) substituted heterocyclyloxy as defined in N<sup>1</sup> herein;
- (32) carboxyl;
- (33) carboxylalkyl wherein alkyl is defined in B herein;
- (34) carboxyl-substituted alkyl wherein substituted alkyl is defined in C herein;
- (35) carboxyl-cycloalkyl wherein cycloalkyl is defined in F herein;

- (36) carboxyl-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
- (37) carboxylaryl wherein aryl is defined in J herein;
- (38) carboxyl-substituted aryl wherein substituted aryl is defined in K herein;
- (39) carboxylheteroaryl wherein heteroaryl is defined in L herein;
- (40) carboxyl-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (41) carboxylheterocyclic wherein heterocyclic is defined in N herein;
- (42) carboxyl-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (43) carboxylamido;
- (44) cyano;
- (45) thiol as defined in X<sup>2</sup> herein;
- (46) thioalkyl as defined in X herein;
- (47) substituted thioalkyl as defined in C42 herein;
- (48) thioaryl as defined in C43 herein;
- (49) substituted thioaryl as defined in C44 herein;
- (50) thioheteroaryl as defined in C47 herein;
- (51) substituted thioheteroaryl as defined in C48 herein;
- (52) thiocycloalkyl as defined in C45 herein;
- (53) substituted thiocycloalkyl as defined in C46 herein;
- (54) thioheterocyclic as defined in C49 herein;
- (55) substituted thioheterocyclic as defined in C50 herein;
- (56) cycloalkyl as defined in F herein;
- (57) substituted cycloalkyl as defined in G herein;
- (58) guanidino as defined in C38 herein;
- (59) guanidinosulfone as defined in C39 herein;



- (60) halo as defined in Q herein;
- (61) nitro;
- (62) heteroaryl as defined in L herein;
- (63) substituted heteroaryl as defined in M herein;
- (64) heterocyclic as defined in N herein;
- (65) substituted heterocyclic as defined in O herein;
- (66) cycloalkoxy as defined in E<sup>1</sup> herein;
- (67) substituted cycloalkoxy as defined in F<sup>1</sup> herein;
- (68) heteroaryloxy as defined in K<sup>1</sup> herein;
- (69) substituted heteroaryloxy as defined in L<sup>1</sup> herein;
- (70) heterocyclyloxy as defined in M<sup>1</sup> herein;
- (71) substituted heterocyclyloxy as defined in N<sup>1</sup> herein;
- (72) oxycarbonylamino as defined in Y<sup>1</sup> herein;
- (73) oxythiocarbonylamino as defined in Z<sup>1</sup> herein;
- (74) -S(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (75) -S(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (76) -S(O)<sub>2</sub>-cycloalkyl wherein cycloalkyl is defined in F herein;
- (77) -S(O)<sub>2</sub>-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
- (78) -S(O)<sub>2</sub>-alkenyl wherein alkenyl is defined in D herein;
- (79) -S(O)<sub>2</sub>-substituted alkenyl wherein substituted alkenyl is defined in E herein;
- (80) -S(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (81) -S(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (82) -S(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;

- (83) -S(O)<sub>2</sub>-substituted heteroaryl wherein substituted aryl is defined in M herein;
- (84) -S(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (85) -S(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (86) -OS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (87) -OS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (88) -OS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (89) -OS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (90) -OS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (91) -OS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (92) -OS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (93) -OS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (94) -OSO<sub>2</sub>-NRR where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;
- (95) -NRS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (96) -NRS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (97) -NRS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (98) -NRS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (99) -NRS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;

- (100)-NRS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (101)-NRS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (102)-NRS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (103)-NRS(O)<sub>2</sub>-NR-alkyl wherein alkyl is defined in B herein;
- (104)-NRS(O)<sub>2</sub>-NR-substituted alkyl wherein substituted alkyl is defined in C herein;
- (105)-NRS(O)<sub>2</sub>-NR-aryl wherein aryl is defined in J herein;
- (106)-NRS(O)<sub>2</sub>-NR-substituted aryl wherein substituted aryl is defined in K herein;
- (107)-NRS(O)<sub>2</sub>-NR-heteroaryl wherein heteroaryl is defined in L herein;
- (108)-NRS(O)<sub>2</sub>-NR-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (109)-NRS(O)<sub>2</sub>-NR-heterocyclic wherein heterocyclic is defined in N herein;
- (110)-NRS(O)<sub>2</sub>-NR-substituted heterocyclic wherein substituted heterocyclic is defined in O herein and where R is:
- (a) hydrogen; or
  - (b) alkyl as defined in B herein;
- (111)mono- and di-alkylamino wherein alkylamino is defined in I<sup>29</sup> herein;
- (112)mono- and di-(substituted alkyl)amino wherein substituted alkylamino is defined in I<sup>210</sup> herein;
- (113)mono- and di-arylamino wherein aryl is defined in J herein and amino is defined in C7 herein;

- (114) mono- and di-substituted arylamino wherein substituted aryl is defined in K herein and amino is defined in C7 herein;
- (115) mono- and di-heteroaryl amino wherein heteroaryl is defined in L herein and amino is defined in C7 herein;
- (116) mono- and di-substituted heteroaryl amino wherein substituted heteroaryl is defined in M herein and amino is defined in C7 herein;
- (117) mono- and di-heterocyclic amino wherein heterocyclic is defined in N herein and amino is defined in C7 herein;
- (118) mono- and di-substituted heterocyclic amino wherein substituted heterocyclic is defined in O herein and amino is defined in C7 herein;
- (119) unsymmetric di-substituted amines having different substituents selected from:
- (a) alkyl as defined in B herein;
  - (b) substituted alkyl as defined in C herein;
  - (c) aryl as defined in J herein;
  - (d) substituted aryl as defined in K herein;
  - (e) heteroaryl as defined in L herein;
  - (f) substituted heteroaryl as defined in M herein;
  - (g) heterocyclic as defined in N herein;
  - (h) substituted heterocyclic as defined in O herein; and
  - (i) amino groups, as defined in C7 herein, on the substituted aryl blocked by conventional blocking groups such as Boc, Cbz, formyl, and the like or substituted with -SO<sub>2</sub>NRR where R is:
    - (i) hydrogen; or
    - (ii) alkyl as defined in B herein;

- (L) heteroaryl of from 2 to 10 carbon atoms and 1 to 4 heteroatoms selected from oxygen, nitrogen and sulfur within the ring or oxides thereof;
- (M) substituted heteroaryl of from 2 to 10 carbon atoms and 1 to 4 heteroatoms selected from oxygen, nitrogen and sulfur within the ring or oxides thereof, which are substituted with from 1 to 3 substituents selected from the group consisting of:
- (1) hydroxy;
  - (2) acyl as defined in R<sup>1</sup> herein;
  - (3) acylamino as defined in S<sup>1</sup> herein;
  - (4) thiocarbonylamino as defined in B<sup>2</sup> herein;
  - (5) acyloxy as defined in T<sup>1</sup> herein;
  - (6) alkyl as defined in B herein;
  - (7) substituted alkyl as defined in C herein;
  - (8) alkoxy as defined in V herein;
  - (9) substituted alkoxy as defined in B<sup>1</sup> herein;
  - (10) alkenyl as defined in D herein;
  - (11) substituted alkenyl as defined in E herein;
  - (12) alkynyl as defined in U herein;
  - (13) substituted alkynyl as defined in Q<sup>231</sup> herein;
  - (14) amidino as defined in C8 herein;
  - (15) alkylamidino wherein alkyl is defined in B herein and amidino is defined in C8 herein;
  - (16) thioamidino as defined in A<sup>2</sup> herein;
  - (17) amino as defined in C7 herein;
  - (18) aminoacyl as defined in U<sup>1</sup> herein;
  - (19) aminocarbonyloxy as defined in X<sup>1</sup> herein;
  - (20) aminocarbonylamino as defined in V<sup>1</sup> herein;

- (21) aminothiocabonylamino as defined in W<sup>1</sup> herein;
- (22) aryl as defined in J herein;
- (23) substituted aryl as defined in K herein;
- (24) aryloxy as defined in I<sup>1</sup> herein;
- (25) substituted aryloxy as defined in J<sup>1</sup> herein;
- (26) cycloalkoxy as defined in E<sup>1</sup> herein;
- (27) substituted cycloalkoxy as defined in F<sup>1</sup> herein;
- (28) heteroaryloxy as defined in K<sup>1</sup> herein;
- (29) substituted heteroaryloxy as defined in L<sup>1</sup> herein;
- (30) heterocyclyloxy as defined in M<sup>1</sup> herein;
- (31) substituted heterocyclyloxy as defined in N<sup>1</sup> herein;
- (32) carboxyl;
- (33) carboxylalkyl wherein alkyl is defined in B herein;
- (34) carboxyl-substituted alkyl wherein substituted alkyl is defined in C herein;
- (35) carboxyl-cycloalkyl wherein cycloalkyl is defined in F herein;
- (36) carboxyl-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
- (37) carboxylaryl wherein aryl is defined in J herein;
- (38) carboxyl-substituted aryl wherein substituted aryl is defined in K herein;
- (39) carboxylheteroaryl wherein heteroaryl is defined in L herein;
- (40) carboxyl-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (41) carboxylheterocyclic wherein heterocyclic is defined in N herein;
- (42) carboxyl-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (43) carboxylamido;

- (44) cyano;
- (45) thiol as defined in X<sup>2</sup> herein;
- (46) thioalkyl as defined in X herein;
- (47) substituted thioalkyl as defined in C42 herein;
- (48) thioaryl as defined in C43 herein;
- (49) substituted thioaryl as defined in C44 herein;
- (50) thioheteroaryl as defined in C47 herein;
- (51) substituted thioheteroaryl as defined in C48 herein;
- (52) thiocycloalkyl as defined in C45 herein;
- (53) substituted thiocycloalkyl as defined in C46 herein;
- (54) thioheterocyclic as defined in C49 herein;
- (55) substituted thioheterocyclic as defined in C50 herein;
- (56) cycloalkyl as defined in F herein;
- (57) substituted cycloalkyl as defined in G herein;
- (58) guanidino as defined in C38 herein;
- (59) guanidinosulfone as defined in C39 herein;
- (60) halo as defined in Q herein;
- (61) nitro;
- (62) heteroaryl as defined in L herein;
- (63) substituted heteroaryl as defined in M herein;
- (64) heterocyclic as defined in N herein;
- (65) substituted heterocyclic as defined in O herein;
- (66) cycloalkoxy as defined in E<sup>1</sup> herein;
- (67) substituted cycloalkoxy as defined in F<sup>1</sup> herein;
- (68) heteroaryloxy as defined in K<sup>1</sup> herein;
- (69) substituted heteroaryloxy as defined in L<sup>1</sup> herein;
- (70) heterocyclyloxy as defined in M<sup>1</sup> herein;
- (71) substituted heterocyclyloxy as defined in N<sup>1</sup> herein;

- (72) oxycarbonylamino as defined in Y<sup>1</sup> herein;
- (73) oxythiocarbonylamino as defined in Z<sup>1</sup> herein;
- (74) -S(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (75) -S(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (76) -S(O)<sub>2</sub>-cycloalkyl wherein cycloalkyl is defined in F herein;
- (77) -S(O)<sub>2</sub>-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
- (78) -S(O)<sub>2</sub>-alkenyl wherein alkenyl is defined in D herein;
- (79) -S(O)<sub>2</sub>-substituted alkenyl wherein substituted alkenyl is defined in E herein;
- (80) -S(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (81) -S(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (82) -S(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (83) -S(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (84) -S(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (85) -S(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (86) -OS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (87) -OS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (88) -OS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (89) -OS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (90) -OS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;



- (91)  $-\text{OS}(\text{O})_2$ -substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (92)  $-\text{OS}(\text{O})_2$ -heterocyclic wherein heterocyclic is defined in N herein;
- (93)  $-\text{OS}(\text{O})_2$ -substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (94)  $-\text{OSO}_2$ -NRR where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;
- (95)  $-\text{NRS}(\text{O})_2$ -alkyl wherein alkyl is defined in B herein;
- (96)  $-\text{NRS}(\text{O})_2$ -substituted alkyl wherein substituted alkyl is defined in C herein;
- (97)  $-\text{NRS}(\text{O})_2$ -aryl wherein aryl is defined in J herein;
- (98)  $-\text{NRS}(\text{O})_2$ -substituted aryl wherein substituted aryl is defined in K herein;
- (99)  $-\text{NRS}(\text{O})_2$ -heteroaryl wherein heteroaryl is defined in L herein;
- (100)  $-\text{NRS}(\text{O})_2$ -substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (101)  $-\text{NRS}(\text{O})_2$ -heterocyclic wherein heterocyclic is defined in N herein;
- (102)  $-\text{NRS}(\text{O})_2$ -substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (103)  $-\text{NRS}(\text{O})_2$ -NR-alkyl wherein alkyl is defined in B herein;
- (104)  $-\text{NRS}(\text{O})_2$ -NR-substituted alkyl wherein substituted alkyl is defined in C herein;
- (105)  $-\text{NRS}(\text{O})_2$ -NR-aryl wherein aryl is defined in J herein;
- (106)  $-\text{NRS}(\text{O})_2$ -NR-substituted aryl wherein substituted aryl is defined in K herein;

- (107)-NRS(O)<sub>2</sub>-NR-heteroaryl wherein heteroaryl is defined in L herein;
- (108)-NRS(O)<sub>2</sub>-NR-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (109)-NRS(O)<sub>2</sub>-NR-heterocyclic wherein heterocyclic is defined in N herein;
- (110)-NRS(O)<sub>2</sub>-NR-substituted heterocyclic wherein substituted heterocyclic is defined in O herein and where R is:
- (a) hydrogen; or
  - (b) alkyl as defined in B herein;
- (111)mono- and di-alkylamino wherein alkylamino is defined in I<sup>29</sup> herein;
- (112)mono- and di-(substituted alkyl)amino wherein substituted alkylamino is defined in I<sup>210</sup> herein;
- (113)mono- and di-arylamino wherein aryl is defined in J herein and amino is defined in C7 herein;
- (114)mono- and di-substituted arylamino wherein substituted aryl is defined in K herein and amino is defined in C7 herein;
- (115)mono- and di-heteroarylamino wherein heteroaryl is defined in L herein and amino is defined in C7 herein;
- (116) mono- and di-substituted heteroarylamino wherein substituted heteroaryl is defined in M herein and amino is defined in C7 herein;
- (117)mono- and di-heterocyclic amino wherein heterocyclic is defined in N herein and amino is defined in C7 herein;
- (118)mono- and di-substituted heterocyclic amino wherein substituted heterocyclic is defined in O herein and amino is defined in C7 herein;

(119) unsymmetric di-substituted amines having different substituents  
selected from:

- (a) alkyl as defined in B herein;
- (b) substituted alkyl as defined in C herein;
- (c) aryl as defined in J herein;
- (d) substituted aryl as defined in K herein;
- (e) heteroaryl as defined in L herein;
- (f) substituted heteroaryl as defined in M herein;
- (g) heterocyclic as defined in N herein;
- (h) substituted heterocyclic as defined in O herein; and
- (i) amino groups, as defined in C7 herein, on the substituted aryl blocked by conventional blocking groups such as Boc, Cbz, formyl, and the like or substituted with -  
SO<sub>2</sub>NRR where R is:
  - (i) hydrogen; or
  - (ii) alkyl as defined in B herein;

(N) heterocyclic of from 1 to 10 carbon atoms and from 1 to 4 heteroatoms selected from nitrogen, sulfur or oxygen within the ring, wherein one or more of the rings can be aryl, as defined in J herein, or heteroaryl as defined in L herein; and

(O) substituted heterocyclic of from 1 to 10 carbon atoms and from 1 to 4 heteroatoms which are substituted with from 1 to 3 substituents selected from the group consisting of:

- (1) oxo (=O);
- (2) thioxo (=S);
- (3) alkoxy as defined in V herein;
- (4) substituted alkoxy as defined in B<sup>1</sup> herein;
- (5) acyl as defined in R<sup>1</sup> herein;

- (6) acylamino as defined in S<sup>1</sup> herein;
- (7) thiocarbonylamino as defined in B<sup>2</sup> herein;
- (8) acyloxy as defined in T<sup>1</sup> herein;
- (9) amino as defined in C7 herein;
- (10) amidino as defined in C8 herein;
- (11) alkylamidino wherein alkyl is defined in B herein and amidino is defined in C8 herein;
- (12) thioamidino as defined in A<sup>2</sup> herein;
- (13) aminoacyl as defined in U<sup>1</sup> herein;
- (14) aminocarbonylamino as defined in V<sup>1</sup> herein;
- (15) aminothiocarbonylamino as defined in W<sup>1</sup> herein;
- (16) aminocarbonyloxy as defined in X<sup>1</sup> herein;
- (17) aryl as defined in J herein;
- (18) substituted aryl as defined in K herein;
- (19) aryloxy as defined in I<sup>1</sup> herein;
- (20) substituted aryloxy as defined in J<sup>1</sup> herein;
- (21) aryloxyaryl as defined in C19 herein;
- (22) substituted aryloxyaryl as defined in C20 herein;
- (23) halogen as defined in Q herein;
- (24) hydroxyl;
- (25) cyano;
- (26) nitro;
- (27) carboxyl;
- (28) carboxylalkyl wherein alkyl is defined in B herein;
- (29) carboxyl-substituted alkyl wherein substituted alkyl is defined in C herein;
- (30) carboxyl-cycloalkyl wherein cycloalkyl is defined in F herein;

- (31) carboxyl-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
- (32) carboxylaryl wherein aryl is defined in J herein;
- (33) carboxyl-substituted aryl wherein substituted aryl is defined in K herein;
- (34) carboxylheteroaryl wherein heteroaryl is defined in L herein;
- (35) carboxyl-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (36) carboxylheterocyclic wherein heterocyclic is defined in N herein;
- (37) carboxyl-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (38) cycloalkyl as defined in F herein;
- (39) substituted cycloalkyl as defined in G herein;
- (40) guanidino as defined in C38 herein;
- (41) guanidinosulfone as defined in C39 herein;
- (42) thiol as defined in X<sup>2</sup> herein;
- (43) thioalkyl as defined in X herein;
- (44) substituted thioalkyl as defined in C42 herein;
- (45) thioaryl as defined in C43 herein;
- (46) substituted thioaryl as defined in C44 herein;
- (47) thiocycloalkyl as defined in C45 herein;
- (48) substituted thiocycloalkyl as defined in C46 herein;
- (49) thioheteroaryl as defined in C47 herein;
- (50) substituted thioheteroaryl as defined in C48 herein;
- (51) thioheterocyclic as defined in C49 herein;
- (52) substituted thioheterocyclic as defined in C50 herein;
- (53) heteroaryl as defined in L herein;
- (54) substituted heteroaryl as defined in M herein;

- (55) heterocyclic as defined in N herein;
- (56) substituted heterocyclic as defined in O herein;
- (57) cycloalkoxy as defined in E<sup>1</sup> herein;
- (58) substituted cycloalkoxy as defined in F<sup>1</sup> herein;
- (59) heteroaryloxy as defined in K<sup>1</sup> herein;
- (60) substituted heteroaryloxy as defined in L<sup>1</sup> herein;
- (61) heterocyclyloxy as defined in M<sup>1</sup> herein;
- (62) substituted heterocyclyloxy as defined in N<sup>1</sup> herein;
- (63) oxycarbonylamino as defined in Y<sup>1</sup> herein;
- (64) oxythiocarbonylamino as defined in Z<sup>1</sup> herein;
- (65) -OS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (66) -OS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (67) -OS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (68) -OS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (69) -OS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (70) -OS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (71) -OS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (72) -OS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (73) -OSO<sub>2</sub>-NRR where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;
- (74) -NRS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (75) -NRS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;

- (76) -NRS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (77) -NRS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (78) -NRS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (79) -NRS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (80) -NRS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (81) -NRS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (82) -NRS(O)<sub>2</sub>-NR-alkyl wherein alkyl is defined in B herein;
- (83) -NRS(O)<sub>2</sub>-NR-substituted alkyl wherein substituted alkyl is defined in C herein;
- (84) -NRS(O)<sub>2</sub>-NR-aryl wherein aryl is defined in J herein;
- (85) -NRS(O)<sub>2</sub>-NR-substituted aryl wherein substituted aryl is defined in K herein;
- (86) -NRS(O)<sub>2</sub>-NR-heteroaryl wherein heteroaryl is defined in L herein;
- (87) -NRS(O)<sub>2</sub>-NR-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (88) -NRS(O)<sub>2</sub>-NR-heterocyclic wherein heterocyclic is defined in N herein;
- (89) -NRS(O)<sub>2</sub>-NR-substituted heterocyclic wherein substituted heterocyclic is defined in O herein and where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;
- (90) mono- and di-alkylamino wherein alkylamino is defined in I<sup>29</sup> herein;

- (91) mono- and di-(substituted alkyl)amino wherein substituted alkylamino is defined in I<sup>2</sup>10 herein;
- (92) mono- and di-arylamino wherein aryl is defined in J herein and amino is defined in C7 herein;
- (93) mono- and di-substituted arylamino wherein substituted aryl is defined in K herein and amino is defined in C7 herein;
- (94) mono- and di-heteroarylamino wherein heteroaryl is defined in L herein and amino is defined in C7 herein;
- (95) mono- and di-substituted heteroarylamino wherein substituted heteroaryl is defined in M herein and amino is defined in C7 herein;
- (96) mono- and di-heterocyclic amino wherein heterocyclic is defined in N herein and amino is defined in C7 herein;
- (97) mono- and di-substituted heterocyclic amino wherein substituted heterocyclic is defined in O herein and amino is defined in C7 herein;
- (98) unsymmetric di-substituted amines having different substituents selected from:
  - (a) alkyl as defined in B herein;
  - (b) substituted alkyl as defined in C herein;
  - (c) aryl as defined in J herein;
  - (d) substituted aryl as defined in K herein;
  - (e) heteroaryl as defined in L herein;
  - (f) substituted heteroaryl as defined in M herein;
  - (g) heterocyclic as defined in N herein;
  - (h) substituted heterocyclic as defined in O herein; and
  - (i) substituted alkynyl groups, wherein substituted alkynyl is defined in Q<sup>2</sup>31 herein, having amino groups blocked by



conventional blocking groups such as Boc, Cbz, formyl, and the like or alkynyl/ groups substituted with:

- (i) -SO<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (ii) -SO<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (iii) -SO<sub>2</sub>-alkenyl wherein alkenyl is defined in D herein;
- (iv) -SO<sub>2</sub>-substituted alkenyl wherein substituted alkenyl is defined in E herein;
- (v) -SO<sub>2</sub>-cycloalkyl wherein cycloalkyl is defined in F herein;
- (vi) -SO<sub>2</sub>-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
- (vii) -SO<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (viii) -SO<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (ix) -SO<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (x) -SO<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (xi) -SO<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (xii) -SO<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein; and
- (xiii) -SO<sub>2</sub>NRR where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;

$R^3$  and  $R^{3a}$  are independently selected from the group consisting of:

- (P) hydrogen;
- (Q) halogen or halo referring to fluoro, chloro, bromo and iodo;
- (R) alkyl as defined in B above;
- (S) substituted alkyl as defined in C above;
- (T) alkenyl as defined in D herein;
- (U) alkynyl of from 2 to 10 carbon atoms and from 1-2 sites of alkynyl unsaturation;
- (V) alkoxy having the formula "alkyl-O-";
- (W) haloalkoxy wherein halo is defined in Q herein and alkoxy is defined in V herein;
- (X) thioalkyl having the formula "-S-alkyl"; or
- (Y)  $-(Alk^b)_mR^b$  in which  $Alk^b$  is a  $C_{1-3}$ alkylene chain, m is 0 or 1 and  $R^b$  is:
  - (1) hydroxy;
  - (2) thiol as defined in X<sup>2</sup> herein;
  - (3) nitro;
  - (4) cyano;
  - (5) carboxy;
  - (6)  $-CO_2R^c$  wherein  $R^c$  is alkyl as defined in B herein;
  - (7)  $-SO_3H$ ;
  - (8)  $-SOR^c$  wherein  $R^c$  is alkyl as defined in B herein;
  - (9)  $-SO_2R^c$  wherein  $R^c$  is alkyl as defined in B herein;
  - (10)  $-SO_3R^c$  wherein  $R^c$  is alkyl as defined in B herein;
  - (11)  $-OCO_2R^c$  wherein  $R^c$  is alkyl as defined in B herein;
  - (12)  $-C(O)H$ ;
  - (13)  $-COR^c$  wherein  $R^c$  is alkyl as defined in B herein;
  - (14)  $-OCOR^c$  wherein  $R^c$  is alkyl as defined in B herein;
  - (15)  $-CSR^c$  wherein  $R^c$  is alkyl as defined in B herein;

- (16)  $-\text{Nr}^{\text{d}}\text{R}^{\text{e}}$  wherein  $\text{R}^{\text{d}}$  and  $\text{R}^{\text{e}}$  are independently hydrogen, alkyl as defined in B herein, or substituted alkyl as defined in C herein;
- (17)  $-\text{CONR}^{\text{d}}\text{R}^{\text{e}}$  wherein  $\text{R}^{\text{d}}$  and  $\text{R}^{\text{e}}$  are independently hydrogen, alkyl as defined in B herein, or substituted alkyl as defined in C herein;
- (18)  $-\text{OCONR}^{\text{d}}\text{R}^{\text{e}}$  wherein  $\text{R}^{\text{d}}$  and  $\text{R}^{\text{e}}$  are independently hydrogen, alkyl as defined in B herein, or substituted alkyl as defined in C herein;
- (19)  $-\text{Nr}^{\text{d}}\text{COR}^{\text{e}}$  wherein  $\text{R}^{\text{d}}$  and  $\text{R}^{\text{e}}$  are independently hydrogen, alkyl as defined in B herein, or substituted alkyl as defined in C herein;
- (20)  $-\text{CSNR}^{\text{d}}\text{R}^{\text{e}}$  wherein  $\text{R}^{\text{d}}$  and  $\text{R}^{\text{e}}$  are independently hydrogen, alkyl as defined in B herein, or substituted alkyl as defined in C herein;
- (21)  $-\text{Nr}^{\text{d}}\text{CSR}^{\text{e}}$  wherein  $\text{R}^{\text{d}}$  and  $\text{R}^{\text{e}}$  are independently hydrogen, alkyl as defined in B herein, or substituted alkyl as defined in C herein;
- (22)  $-\text{SO}_2\text{NR}^{\text{d}}\text{R}^{\text{e}}$  wherein  $\text{R}^{\text{d}}$  and  $\text{R}^{\text{e}}$  are independently hydrogen, alkyl as defined in B herein, or substituted alkyl as defined in C herein;
- (23)  $-\text{Nr}^{\text{d}}\text{SO}_2\text{R}^{\text{e}}$  wherein  $\text{R}^{\text{d}}$  and  $\text{R}^{\text{e}}$  are independently hydrogen, alkyl as defined in B herein, or substituted alkyl as defined in C herein;
- (24)  $-\text{Nr}^{\text{d}}\text{CONR}^{\text{e}}\text{R}^{\text{f}}$  wherein  $\text{R}^{\text{d}}$  and  $\text{R}^{\text{e}}$  are independently hydrogen, alkyl as defined in B herein, or substituted alkyl as defined in C herein; and where  $\text{R}^{\text{f}}$  is hydrogen alkyl as defined in B herein, or substituted alkyl as defined in C herein; or
- (25)  $-\text{Nr}^{\text{d}}\text{SO}_2\text{NR}^{\text{e}}\text{R}^{\text{f}}$  wherein  $\text{R}^{\text{d}}$  and  $\text{R}^{\text{e}}$  are independently hydrogen, alkyl as defined in B herein, or substituted alkyl as defined in C herein; and where  $\text{R}^{\text{f}}$  is hydrogen, alkyl as defined in B herein, or substituted alkyl as defined in C herein.

X is selected from the group consisting of:

- (Z) hydroxyl;
- (A<sup>1</sup>) alkoxy as defined in V herein;

- (B<sup>1</sup>) substituted alkoxy having the formula "substituted alkyl-O-";
- (C<sup>1</sup>) alkenoxy having the formula "alkenyl-O-";
- (D<sup>1</sup>) substituted alkenoxy having the formula "substituted alkenyl-O-";
- (E<sup>1</sup>) cycloalkoxy having the formula "-O-cycloalkyl";
- (F<sup>1</sup>) substituted cycloalkoxy having the formula "-O-substituted cycloalkyl";
- (G<sup>1</sup>) cycloalkenoxyl having the formula "-O-cycloalkenyl";
- (H<sup>1</sup>) substituted cycloalkenoxyl having the formula "-O-substituted cycloalkenyl";
- (I<sup>1</sup>) aryloxy having the formula "aryl-O-";
- (J<sup>1</sup>) substituted aryloxy having the formula "substituted aryl-O-";
- (K<sup>1</sup>) heteroaryloxy having the formula "-O-heteroaryl";
- (L<sup>1</sup>) substituted heteroaryloxy having the formula "-O-substituted heteroaryl";
- (M<sup>1</sup>) heterocyclyloxy having the formula "-O-heterocyclic";
- (N<sup>1</sup>) substituted heterocyclyloxy having the formula "-O-substituted heterocyclic"; and
- (O<sup>1</sup>) -NR"R" where each R" is independently selected from the group consisting of:
  - (1) hydrogen;
  - (2) alkyl as defined in B herein;
  - (3) substituted alkyl as defined in C herein;
  - (4) alkenyl as defined in D herein;
  - (5) substituted alkenyl as defined in E herein;
  - (6) cycloalkyl as defined in F herein;
  - (7) substituted cycloalkyl as defined in G herein;
  - (8) aryl as defined in J herein;
  - (9) substituted aryl as defined in K herein;
  - (10) heteroaryl as defined in L herein;

- (11) substituted heteroaryl as defined in M herein;
- (12) heterocyclic as defined in N herein; and
- (13) substituted heterocyclic as defined in O herein;

R<sup>2a</sup> is either:

- (i) an -Ar<sup>1</sup>-R<sup>9</sup> group where Ar<sup>1</sup> is:
  - (P<sup>1</sup>) aryl as defined in J herein; or
  - (Q<sup>1</sup>) heteroaryl, as defined in L herein, optionally substituted with one or two substituents selected from the group consisting of:
    - (1) hydroxy;
    - (2) acyl as defined in R<sup>1</sup> herein;
    - (3) acylamino as defined in S<sup>1</sup> herein;
    - (4) aminoacyl as defined in U<sup>1</sup> herein;
    - (5) acyloxy as defined in T<sup>1</sup> herein;
    - (6) alkyl as defined in B herein;
    - (7) substituted alkyl as defined in C herein;
    - (8) alkoxy as defined in V herein;
    - (9) substituted alkoxy as defined in B<sup>1</sup> herein;
    - (10) amino as defined in C7 herein;
    - (11) aminoacyl as defined in U<sup>1</sup> herein;
    - (12) aminocarbonyloxy as defined in X<sup>1</sup> herein;
    - (13) carboxyl;
    - (14) carboxylalkyl wherein alkyl is defined in B herein;
    - (15) carboxylamido;
    - (16) cyano;
    - (17) thiol as defined in X<sup>2</sup> herein;
    - (18) thioalkyl as defined in X herein;
    - (19) substituted thioalkyl as defined in C42 herein;
    - (20) halo as defined in Q herein;
    - (21) nitro;

provided that said acyl, acylamino, acyloxy, substituted alkyl, substituted alkoxy and substituted thioalkyl do not carry an aryl, substituted aryl, heteroaryl or substituted heteroaryl group; and

R<sup>9</sup> is selected from the group consisting of:

- (R<sup>1</sup>) acyl selected from H-C(O)-, alkyl-C(O)-, substituted alkyl-C(O)-, alkenyl-C(O)-, substituted alkenyl-C(O)-, alkynyl-C(O)-, substituted alkynyl-C(O)-, cycloalkyl-C(O)-, substituted cycloalkyl-C(O)-, aryl-C(O)-, substituted aryl-C(O)-, heteroaryl-C(O)-, substituted heteroaryl-C(O), heterocyclic-C(O)-, and substituted heterocyclic-C(O)-, wherein alkyl is defined in B herein; wherein substituted alkyl is defined in C herein; wherein alkenyl is defined in D herein; wherein substituted alkenyl is defined in E herein; wherein alkynyl is defined in U herein; wherein substituted alkynyl is defined in Q<sup>2</sup>31 herein; wherein cycloalkyl is defined in F herein; wherein substituted cycloalkyl is defined in G herein; wherein aryl is defined in J herein; wherein substituted aryl is defined in K herein; wherein heteroaryl is defined in L herein; wherein substituted heteroaryl is defined in M herein; wherein heterocyclic is defined in N herein; and wherein substituted heterocyclic is defined in O herein;
- (S<sup>1</sup>) acylamino selected from the group -C(O)NRR where each R is independently selected from the group consisting of:
- (1) hydrogen;
  - (2) alkyl as defined in B herein;
  - (3) substituted alkyl as defined in C herein;
  - (4) alkenyl as defined in D herein;
  - (5) substituted alkenyl as defined in E herein;
  - (6) alkynyl as defined in U herein;
  - (7) substituted alkynyl as defined in Q<sup>2</sup>31 herein;
  - (8) aryl as defined in J herein;

- (9) substituted aryl as defined in K herein;
- (10) cycloalkyl as defined in F herein;
- (11) substituted cycloalkyl as defined in G herein;
- (12) heteroaryl as defined in L herein;
- (13) substituted heteroaryl as defined in M herein;
- (14) heterocyclic as defined in N herein;
- (15) substituted heterocyclic as defined in O herein; and

where each R is joined to form together with the nitrogen atom a heterocyclic or substituted heterocyclic ring wherein alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic are as defined herein.

- (T<sup>1</sup>) acyloxy selected from the groups alkyl-C(O)O-, substituted alkyl-C(O)O-, alkenyl-C(O)O-, substituted alkenyl-C(O)O-, alkynyl-C(O)O-, substituted alkynyl-C(O)O-, aryl-C(O)O-, substituted aryl-C(O)O-, cycloalkyl-C(O)O-, substituted cycloalkyl-C(O)O-, heteroaryl-C(O)O-, substituted heteroaryl-C(O)O-, heterocyclic-C(O)O-, and substituted heterocyclic-C(O)O-wherein alkyl is defined in B herein; wherein substituted alkyl is defined in C herein; wherein alkenyl is defined in D herein; wherein substituted alkenyl is defined in E herein; wherein alkynyl is defined in U herein; wherein substituted alkynyl is defined in Q<sup>231</sup> herein; wherein cycloalkyl is defined in F herein; wherein substituted cycloalkyl is defined in G herein; wherein aryl is defined in J herein; wherein substituted aryl is defined in K herein; wherein heteroaryl is defined in L herein; wherein substituted heteroaryl is defined in M herein; wherein heterocyclic is defined in N herein; and wherein substituted heterocyclic is defined in O herein;
- (U<sup>1</sup>) aminoacyl having the formula -NRC(O)alkyl, -NRC(O)substituted alkyl, -NRC(O)cycloalkyl, -NRC(O)substituted cycloalkyl, -

NRC(O)alkenyl, -NRC(O)substituted alkenyl, -NRC(O)alkynyl, -  
NRC(O)substituted alkynyl, -NRC(O)aryl, -NRC(O)substituted aryl, -  
NRC(O)heteroaryl, -NRC(O) substituted heteroaryl, -  
NRC(O)heterocyclic, and -NRC(O)substituted heterocyclic where R is  
hydrogen or alkyl and wherein alkyl is defined in B herein; wherein  
substituted alkyl is defined in C herein; wherein alkenyl is defined in D  
herein; wherein substituted alkenyl is defined in E herein; wherein  
alkynyl is defined in U herein; wherein substituted alkynyl is defined  
in Q<sup>231</sup> herein; wherein cycloalkyl is defined in F herein; wherein  
substituted cycloalkyl is defined in G herein; wherein aryl is defined in  
J herein; wherein substituted aryl is defined in K herein; wherein  
heteroaryl is defined in L herein; wherein substituted heteroaryl is  
defined in M herein; wherein heterocyclic is defined in N herein; and  
wherein substituted heterocyclic is defined in O herein;

(V<sup>1</sup>) aminocarbonylamino formula -NRC(O)NRR, -NRC(O)NR-alkyl, -  
NRC(O)NR-substituted alkyl, -NRC(O)NR-alkenyl, -NRC(O)NR-  
substituted alkenyl, -NRC(O)NR-alkynyl, -NRC(O)NR-substituted  
alkynyl, -NRC(O)NR-aryl, -NRC(O)NR-substituted aryl, -  
NRC(O)NR-cycloalkyl, -NRC(O)NR-substituted cycloalkyl, -  
NRC(O)NR-heteroaryl, and -NRC(O)NR-substituted heteroaryl, -  
NRC(O)NR-heterocyclic, and -NRC(O)NR-substituted heterocyclic  
where each R is independently hydrogen, alkyl or where each R is  
joined to form together with the nitrogen atom a heterocyclic or  
substituted heterocyclic ring as well as where one of the amino groups  
is blocked by conventional blocking groups such as Boc, Cbz, formyl,  
and the like and wherein alkyl is defined in B herein; wherein  
substituted alkyl is defined in C herein; wherein alkenyl is defined in D  
herein; wherein substituted alkenyl is defined in E herein; wherein  
alkynyl is defined in U herein; wherein substituted alkynyl is defined



in Q<sup>2</sup>31 herein; wherein cycloalkyl is defined in F herein; wherein substituted cycloalkyl is defined in G herein; wherein aryl is defined in J herein; wherein substituted aryl is defined in K herein; wherein heteroaryl is defined in L herein; wherein substituted heteroaryl is defined in M herein; wherein heterocyclic is defined in N herein; and wherein substituted heterocyclic is defined in O herein;

- (W<sup>1</sup>) aminothiocabonylamino having the formula -NRC(S)NRR, -NRC(S)NR-alkyl, -NRC(S)NR-substituted alkyl, -NRC(S)NR-alkenyl, -NRC(S)NR-substituted alkenyl, -NRC(S)NR-alkynyl, -NRC(S)NR-substituted alkynyl, -NRC(S)NR-aryl, -NRC(S)NR-substituted aryl, -NRC(S)NR-cycloalkyl, -NRC(S)NR-substituted cycloalkyl, -NRC(S)NR-heteroaryl, and -NRC(S)NR-substituted heteroaryl, -NRC(S)NR-heterocyclic, and -NRC(S)NR-substituted heterocyclic where each R is independently hydrogen, alkyl or where each R is joined to form together with the nitrogen atom a heterocyclic or substituted heterocyclic ring as well as where one of the amino groups is blocked by conventional blocking groups such as Boc, Cbz, formyl, and the like and wherein alkyl is defined in B herein; wherein substituted alkyl is defined in C herein; wherein alkenyl is defined in D herein; wherein substituted alkenyl is defined in E herein; wherein alkynyl is defined in U herein; wherein substituted alkynyl is defined in Q<sup>2</sup>31 herein; wherein cycloalkyl is defined in F herein; wherein substituted cycloalkyl is defined in G herein; wherein aryl is defined in J herein; wherein substituted aryl is defined in K herein; wherein heteroaryl is defined in L herein; wherein substituted heteroaryl is defined in M herein; wherein heterocyclic is defined in N herein; and wherein substituted heterocyclic is defined in O herein;
- (X<sup>1</sup>) aminocarbonyloxy having the formula -NRC(O)O-alkyl, -NRC(O)O-substituted alkyl, -NRC(O)O-alkenyl, -NRC(O)O-substituted alkenyl, -

NRC(O)O-alkynyl, -NRC(O)O-substituted alkynyl, -NRC(O)O-cycloalkyl, -NRC(O)O-substituted cycloalkyl, -NRC(O)O-aryl, -NRC(O)O-substituted aryl, -NRC(O)O-heteroaryl, -NRC(O)O-substituted heteroaryl, -NRC(O)O-heterocyclic, and -NRC(O)O-substituted heterocyclic where R is hydrogen or alkyl and wherein alkyl is defined in B herein; wherein substituted alkyl is defined in C herein; wherein alkenyl is defined in D herein; wherein substituted alkenyl is defined in E herein; wherein alkynyl is defined in U herein; wherein substituted alkynyl is defined in Q<sup>2</sup>31 herein; wherein cycloalkyl is defined in F herein; wherein substituted cycloalkyl is defined in G herein; wherein aryl is defined in J herein; wherein substituted aryl is defined in K herein; wherein heteroaryl is defined in L herein; wherein substituted heteroaryl is defined in M herein; wherein heterocyclic is defined in N herein; and wherein substituted heterocyclic is defined in O herein;

(Y<sup>1</sup>) oxycarbonylamino having the formula -OC(O)NH<sub>2</sub>, -OC(O)NRR, -OC(O)NR-alkyl, -OC(O)NR-substituted alkyl, -OC(O)NR-alkenyl, -OC(O)NR-substituted alkenyl, -OC(O)NR-alkynyl, -OC(O)NR-substituted alkynyl, -OC(O)NR-cycloalkyl, -OC(O)NR-substituted cycloalkyl, -OC(O)NR-aryl, -OC(O)NR-substituted aryl, -OC(O)NR-heteroaryl, -OC(O)NR-substituted heteroaryl, -OC(O)NR-heterocyclic, and -OC(O)NR-substituted heterocyclic where R is hydrogen, alkyl or where each R is joined to form, together with the nitrogen atom a heterocyclic or substituted heterocyclic ring and wherein alkyl is defined in B herein; wherein substituted alkyl is defined in C herein; wherein alkenyl is defined in D herein; wherein substituted alkenyl is defined in E herein; wherein alkynyl is defined in U herein; wherein substituted alkynyl is defined in Q<sup>2</sup>31 herein; wherein cycloalkyl is defined in F herein; wherein substituted cycloalkyl is defined in G

herein; wherein aryl is defined in J herein; wherein substituted aryl is defined in K herein; wherein heteroaryl is defined in L herein; wherein substituted heteroaryl is defined in M herein; wherein heterocyclic is defined in N herein; and wherein substituted heterocyclic is defined in O herein;

- (Z<sup>1</sup>) oxythiocarbonylamino having the formula -OC(S)NH<sub>2</sub>, -OC(S)NRR, -OC(S)NR-alkyl, -OC(S)NR-substituted alkyl, -OC(S)NR-alkenyl, -OC(S)NR-substituted alkenyl, -OC(S)NR-alkynyl, -OC(S)NR-substituted alkynyl, -OC(S)NR-cycloalkyl, -OC(S)NR-substituted cycloalkyl, -OC(S)NR-aryl, -OC(S)NR-substituted aryl, -OC(S)NR-heteroaryl, -OC(S)NR-substituted heteroaryl, -OC(S)NR-heterocyclic, and -OC(S)NR-substituted heterocyclic where R is hydrogen, alkyl or where each R is joined to form together with the nitrogen atom a heterocyclic or substituted heterocyclic ring and wherein alkyl is defined in B herein; wherein substituted alkyl is defined in C herein; wherein alkenyl is defined in D herein; wherein substituted alkenyl is defined in E herein; wherein alkynyl is defined in U herein; wherein substituted alkynyl is defined in Q<sup>2</sup>31 herein; wherein cycloalkyl is defined in F herein; wherein substituted cycloalkyl is defined in G herein; wherein aryl is defined in J herein; wherein substituted aryl is defined in K herein; wherein heteroaryl is defined in L herein; wherein substituted heteroaryl is defined in M herein; wherein heterocyclic is defined in N herein; and wherein substituted heterocyclic is defined in O herein;
- (A<sup>2</sup>) thioamidino having the formula "RSC(=NH)-";
- (B<sup>2</sup>) thiocarbonylamino selected from the group -C(S)NRR where each R is independently selected from the group consisting of:
- (1) hydrogen;
  - (2) alkyl as defined in B herein;

- (3) substituted alkyl as defined in C herein;
- (4) alkenyl as defined in D herein;
- (5) substituted alkenyl as defined in E herein;
- (6) alkynyl as defined in U herein;
- (7) substituted alkynyl as defined in Q<sup>231</sup> herein;
- (8) aryl as defined in J herein;
- (9) substituted aryl as defined in K herein;
- (10) cycloalkyl as defined in F herein;
- (11) substituted cycloalkyl as defined in G herein;
- (12) heteroaryl as defined in L herein;
- (13) substituted heteroaryl as defined in M herein;
- (14) heterocyclic as defined in N herein;
- (15) substituted heterocyclic as defined in O herein; and

where each R is joined to form, together with the nitrogen atom a heterocyclic or substituted heterocyclic ring wherein alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, and substituted heterocyclic are as defined herein;

- (C<sup>2</sup>) aminosulfonylamino having the formula -NRSO<sub>2</sub>NRR, -NRSO<sub>2</sub>NR-alkyl, -NRSO<sub>2</sub>NR-substituted alkyl, -NRSO<sub>2</sub>NR-alkenyl, -NRSO<sub>2</sub>NR-substituted alkenyl, -NRSO<sub>2</sub>NR-alkynyl, -NRSO<sub>2</sub>NR-substituted alkynyl, -NRSO<sub>2</sub>NR-aryl, -NRSO<sub>2</sub>NR-substituted aryl, -NRSO<sub>2</sub>NR-cycloalkyl, -NRSO<sub>2</sub>NR-substituted cycloalkyl, -NRSO<sub>2</sub>NR-heteroaryl, and -NRSO<sub>2</sub>NR-substituted heteroaryl, -NRSO<sub>2</sub>NR-heterocyclic, and -NRSO<sub>2</sub>NR-substituted heterocyclic, where each R is independently hydrogen, alkyl or where each R is joined to form together with the nitrogen atom a heterocyclic or substituted heterocyclic ring as well as where one of the amino groups is blocked by conventional blocking groups such as Boc, Cbz, formyl, and the like and wherein alkyl is

defined in B herein; wherein substituted alkyl is defined in C herein; wherein alkenyl is defined in D herein; wherein substituted alkenyl is defined in E herein; wherein alkynyl is defined in U herein; wherein substituted alkynyl is defined in Q<sup>2</sup>31 herein; wherein cycloalkyl is defined in F herein; wherein substituted cycloalkyl is defined in G herein; wherein aryl is defined in J herein; wherein substituted aryl is defined in K herein; wherein heteroaryl is defined in L herein; wherein substituted heteroaryl is defined in M herein; wherein heterocyclic is defined in N herein; and wherein substituted heterocyclic is defined in O herein;

- (D<sup>2</sup>) aminosulfonyloxy having the formula -NRSO<sub>2</sub>O-alkyl, -NRSO<sub>2</sub>O-substituted alkyl, -NRSO<sub>2</sub>O-alkenyl, -NRSO<sub>2</sub>O-substituted alkenyl, -NRSO<sub>2</sub>O-alkynyl, -NRSO<sub>2</sub>O-substituted alkynyl, -NRSO<sub>2</sub>O-cycloalkyl, -NRSO<sub>2</sub>O-substituted cycloalkyl, -NRSO<sub>2</sub>O-aryl, -NRSO<sub>2</sub>O-substituted aryl, -NRSO<sub>2</sub>O-heteroaryl, -NRSO<sub>2</sub>O-substituted heteroaryl, -NRSO<sub>2</sub>O-heterocyclic, and -NRSO<sub>2</sub>O-substituted heterocyclic where R is hydrogen or alkyl and wherein alkyl is defined in B herein; wherein substituted alkyl is defined in C herein; wherein alkenyl is defined in D herein; wherein substituted alkenyl is defined in E herein; wherein alkynyl is defined in U herein; wherein substituted alkynyl is defined in Q<sup>2</sup>31 herein; wherein cycloalkyl is defined in F herein; wherein substituted cycloalkyl is defined in G herein; wherein aryl is defined in J herein; wherein substituted aryl is defined in K herein; wherein heteroaryl is defined in L herein; wherein substituted heteroaryl is defined in M herein; wherein heterocyclic is defined in N herein; and wherein substituted heterocyclic is defined in O herein;
- (E<sup>2</sup>) aminosulfonyl having the formula -NRSO<sub>2</sub>alkyl, -NRSO<sub>2</sub>substituted alkyl, -NRSO<sub>2</sub>cycloalkyl, -NRSO<sub>2</sub>substituted cycloalkyl, -NRSO<sub>2</sub>alkenyl, -NRSO<sub>2</sub>substituted alkenyl, -NRSO<sub>2</sub>alkynyl, -

NRSO<sub>2</sub>substituted alkynyl, -NRSO<sub>2</sub>aryl, -NRSO<sub>2</sub>substituted aryl, -NRSO<sub>2</sub>heteroaryl, -NRSO<sub>2</sub>substituted heteroaryl, -NRSO<sub>2</sub>heterocyclic, and -NRSO<sub>2</sub>substituted heterocyclic where R is hydrogen or alkyl and wherein alkyl is defined in B herein; wherein substituted alkyl is defined in C herein; wherein alkenyl is defined in D herein; wherein substituted alkenyl is defined in E herein; wherein alkynyl is defined in U herein; wherein substituted alkynyl is defined in Q<sup>231</sup> herein; wherein cycloalkyl is defined in F herein; wherein substituted cycloalkyl is defined in G herein; wherein aryl is defined in J herein; wherein substituted aryl is defined in K herein; wherein heteroaryl is defined in L herein; wherein substituted heteroaryl is defined in M herein; wherein heterocyclic is defined in N herein; and wherein substituted heterocyclic is defined in O herein;

- (F<sup>2</sup>) oxysulfonylamino having the formula -OSO<sub>2</sub>NH<sub>2</sub>, -OSO<sub>2</sub>NRR-, -OSO<sub>2</sub>NR-alkyl, -OSO<sub>2</sub>NR-substituted alkyl, -OSO<sub>2</sub>NR-alkenyl, -OSO<sub>2</sub>NR-substituted alkenyl, -OSO<sub>2</sub>NR-alkynyl, -OSO<sub>2</sub>NR-substituted alkynyl, -OSO<sub>2</sub>NR-cycloalkyl, -OSO<sub>2</sub>NR-substituted cycloalkyl, -OSO<sub>2</sub>NR-aryl, -OSO<sub>2</sub>NR-substituted aryl, -OSO<sub>2</sub>NR-heteroaryl, -OSO<sub>2</sub>NR-substituted heteroaryl, -OSO<sub>2</sub>NR-heterocyclic, and -OSO<sub>2</sub>NR-substituted heterocyclic where R is hydrogen, alkyl or where each R is joined to form, together with the nitrogen atom a heterocyclic or substituted heterocyclic ring and wherein alkyl is defined in B herein; wherein substituted alkyl is defined in C herein; wherein alkenyl is defined in D herein; wherein substituted alkenyl is defined in E herein; wherein alkynyl is defined in U herein; wherein substituted alkynyl is defined in Q<sup>231</sup> herein; wherein cycloalkyl is defined in F herein; wherein substituted cycloalkyl is defined in G herein; wherein aryl is defined in J herein; wherein substituted aryl is defined in K herein; wherein heteroaryl is defined in L herein; wherein substituted

heteroaryl is defined in M herein; wherein heterocyclic is defined in N herein; and wherein substituted heterocyclic is defined in O herein; and  
(G<sup>2</sup>) oxysulfonyl selected from the groups alkyl-SO<sub>2</sub>O-, substituted alkyl-SO<sub>2</sub>O-, alkenyl-SO<sub>2</sub>O-, substituted alkenyl-SO<sub>2</sub>O-, alkynyl-SO<sub>2</sub>O-, substituted alkynyl-SO<sub>2</sub>O-, aryl-SO<sub>2</sub>O-, substituted aryl-SO<sub>2</sub>O-, cycloalkyl-SO<sub>2</sub>O-, substituted cycloalkyl-SO<sub>2</sub>O-, heteroaryl-SO<sub>2</sub>O-, substituted heteroaryl-SO<sub>2</sub>O-, heterocyclic-SO<sub>2</sub>O-, and substituted heterocyclic-SO<sub>2</sub>O- wherein alkyl is defined in B herein; wherein substituted alkyl is defined in C herein; wherein alkenyl is defined in D herein; wherein substituted alkenyl is defined in E herein; wherein alkynyl is defined in U herein; wherein substituted alkynyl is defined in Q<sup>231</sup> herein; wherein cycloalkyl is defined in F herein; wherein substituted cycloalkyl is defined in G herein; wherein aryl is defined in J herein; wherein substituted aryl is defined in K herein; wherein heteroaryl is defined in L herein; wherein substituted heteroaryl is defined in M herein; wherein heterocyclic is defined in N herein; and wherein substituted heterocyclic is defined in O herein;

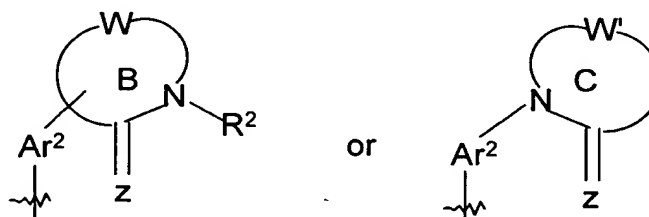
provided that when R<sup>9</sup> is acylamino or acyloxy then the acylamino or acyloxy group does not carry an aryl, substituted aryl, heteroaryl or substituted heteroaryl group; or

(ii) a group of formula (a) or (b):

wherein:

Ar<sup>2</sup> is an:

(H<sup>2</sup>) aryl as defined in J herein; or



- (I<sup>2</sup>) heteroaryl group optionally substituted, in addition to ring B or C, with one or two substituent(s) selected from the group consisting of:
- (1) hydrogen;
  - (2) halogen as defined in Q herein;
  - (3) hydroxy;
  - (4) alkoxy as defined in V herein;
  - (5) substituted alkoxy as defined in B<sup>1</sup> herein;
  - (6) acyloxy as defined in T<sup>1</sup> herein;
  - (7) substituted acyloxy;
  - (8) amino as defined in C7 herein;
  - (9) alkylamino having the formula -NHR wherein R is alkyl as defined in B herein;
  - (10) substituted alkylamino having the formula -NHR wherein R is substituted alkyl as defined in C herein;
  - (11) dialkylamino having the formula -NRR wherein each R is alkyl as defined in B herein;
  - (12) substituted dialkylamino having the formula -NRR wherein each R is substituted alkyl as defined in C herein;
  - (13) acylamino as defined in S<sup>1</sup> herein;
  - (14) substituted acylamino;
  - (15) N-acyl-N-alkylamino wherein acyl is defined in R<sup>1</sup> herein and alkylamino is defined in I<sup>29</sup> herein;
  - (16) substituted N-acyl-N-alkylamino wherein acyl is defined in R<sup>1</sup> herein and substituted alkylamino is defined in I<sup>210</sup> herein;
  - (17) (alkylsulfonyl)amino wherein alkylsulfonyl is defined in C<sup>3</sup> herein and amino is defined in C7 herein;
  - (18) substituted (alkylsulfonyl)amino wherein substituted alkylsulfonyl is defined in D<sup>3</sup> herein and amino is defined in C7 herein;



- (19) N-(alkylsulfonyl)-N-alkylamino wherein alkylsulfonyl is defined in C<sup>3</sup> herein and alkylamino is defined in I<sup>2</sup>9 herein;
- (20) substituted N-(alkylsulfonyl)-N-alkylamino wherein substituted alkylsulfonyl is defined in D<sup>3</sup> herein and substituted alkylamino is defined in I<sup>2</sup>10 herein;
- (21) alkyl as defined in B herein;
- (22) substituted alkyl as defined in C herein;
- (23) cycloalkyl as defined in F herein;
- (24) substituted cycloalkyl as defined in G herein;
- (25) alkenyl as defined in D herein;
- (26) substituted alkenyl as defined in E herein;
- (27) cycloalkenyl as defined in H herein;
- (28) substituted cycloalkenyl as defined in I herein;
- (29) alkynyl as defined in U herein;
- (30) substituted alkynyl as defined in Q<sup>2</sup>31 herein;
- (31) cyano;
- (32) acyl as defined in R<sup>1</sup> herein;
- (33) substituted acyl;
- (34) carboxy;
- (35) substituted carboxy;
- (36) thiol as defined in X<sup>2</sup> herein;
- (37) alkylthio as defined in X herein;
- (38) substituted alkylthio as defined in Z<sup>2</sup> herein;
- (39) alkylsulfoxy as defined in A<sup>3</sup> herein;
- (40) substituted alkylsulfoxy as defined in B<sup>3</sup> herein;
- (41) alkylsulfonyl as defined in C<sup>3</sup> herein; and
- (42) substituted alkylsulfonyl as defined in D<sup>3</sup> herein;

Z is -O- or -S-;

B is a group wherein W, together with  $-C(=Z)NR^2-$ , forms a saturated or unsaturated heterocyclic group, wherein heterocyclic is defined in N herein, containing 2 to 5 carbon atoms and 0 to 4 additional heteroatoms selected from the group consisting of:

- (J<sup>2</sup>) nitrogen;
- (K<sup>2</sup>) oxygen; and
- (L<sup>2</sup>)  $-So_n-$  (where n is 0 to 2);

wherein said saturated or unsaturated heterocyclic group is optionally fused with one or two ring(s) structures selected from the group consisting of:

- (M<sup>2</sup>) cycloalkyl as defined in F herein;
- (N<sup>2</sup>) cycloalkenyl as defined in H herein;
- (O<sup>2</sup>) heterocyclic as defined in N herein;
- (P<sup>2</sup>) aryl as defined in J herein; and
- (Q<sup>2</sup>) heteroaryl group, wherein heteroaryl is as defined in L herein, to form a bi- or tri-fused ring system and further wherein said heterocyclic group and each of such ring structures are optionally substituted with 1 to 3 substituents selected from the group consisting of with one or two substituent(s) selected from the group consisting of:

- (1) hydrogen;
- (2) halogen as defined in Q herein;
- (3) hydroxy;
- (4) alkoxy as defined in V herein;
- (5) substituted alkoxy as defined in B<sup>1</sup> herein;
- (6) acyloxy as defined in T<sup>1</sup> herein;
- (7) substituted acyloxy;
- (8) amino as defined in C<sup>7</sup> herein;
- (9) alkylamino as defined in I<sup>2</sup>9 herein;
- (10) substituted alkylamino as defined in I<sup>2</sup>10 herein;
- (11) dialkylamino as defined in I<sup>2</sup>11 herein;

- (12) substituted dialkylamino as defined in I<sup>2</sup>12 herein;
- (13) acylamino as defined in S<sup>1</sup> herein;
- (14) substituted acylamino;
- (15) N-acyl-N-alkylamino wherein acyl is defined in R<sup>1</sup> herein and alkylamino I<sup>2</sup>9 herein;
- (16) substituted N-acyl-N-alkylamino wherein acyl is defined in R<sup>1</sup> herein and substituted alkylamino is defined in I<sup>2</sup>10 herein;
- (17) alkylene dioxy;
- (18) (alkylsulfonyl)amino wherein alkylsulfonyl is defined in C<sup>3</sup> herein and amino is define in C7 herein;
- (19) substituted (alkylsulfonyl)amino wherein substituted alkylsulfonyl is defined in D<sup>3</sup> herein and amino is defined in C7 herein;
- (20) N-(alkylsulfonyl)-N-alkylamino wherein alkylsulfonyl is defined in C<sup>3</sup> herein and alkylamino is defined in I<sup>2</sup>9 herein;
- (21) substituted N-(alkylsulfonyl)-N-alkylamino wherein substituted alkylsulfonyl is defined in D<sup>3</sup> herein and substituted alkylamino is defined in I<sup>2</sup>10 herein;
- (22) alkyl as defined in B herein;
- (23) substituted alkyl as defined in C herein;
- (24) cycloalkyl as defined in F herein;
- (25) substituted cycloalkyl as defined in G herein;
- (26) alkenyl as defined in D herein;
- (27) substituted alkenyl as defined in E herein;
- (28) cycloalkenyl as defined in H herein;
- (29) substituted cycloalkenyl as defined in I herein;
- (30) alkynyl as defined in U herein;
- (31) substituted alkynyl having from 1 to 5 substituents selected from the group consisting of:

- (a) alkoxy as defined in V herein;
- (b) substituted alkoxy as defined in B<sup>1</sup> herein;
- (c) acyl as defined in R<sup>1</sup> herein;
- (d) acylamino as defined in S<sup>1</sup> herein;
- (e) thiocarbonylamino as defined in B<sup>2</sup> herein;
- (f) acyloxy as defined in T<sup>1</sup> herein;
- (g) amino as defined in C7 herein;
- (h) amidino as defined in C8 herein;
- (i) alkylamidino wherein alkyl is defined in B herein and amidino is defined in C8 herein;
- (j) thioamidino as defined in A<sup>2</sup> herein;
- (k) aminoacyl as defined in U<sup>1</sup> herein;
- (l) aminocarbonylamino as defined in V<sup>1</sup> herein;
- (m) aminothiocarbonylamino as defined in W<sup>1</sup> herein;
- (n) aminocarbonyloxy as defined in X<sup>1</sup> herein;
- (o) aryl as defined in J herein;
- (p) substituted aryl as defined in K herein;
- (q) aryloxy as defined in I<sup>1</sup> herein;
- (r) substituted aryloxy as defined in J<sup>1</sup> herein;
- (s) aryloxyaryl as defined in C19 herein;
- (t) substituted aryloxyaryl as defined in C20 herein;
- (u) halogen as defined in Q herein;
- (v) hydroxyl;
- (w) cyano;
- (x) nitro;
- (y) carboxyl;
- (z) carboxylalkyl wherein alkyl is defined in B herein;
- (a<sup>1</sup>) carboxyl-substituted alkyl wherein substituted alkyl is defined in C herein;

- (b<sup>1</sup>) carboxyl-cycloalkyl wherein cycloalkyl is defined in F herein;
- (c<sup>1</sup>) carboxyl-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
- (d<sup>1</sup>) carboxylaryl wherein aryl is defined in J herein;
- (e<sup>1</sup>) carboxyl-substituted aryl wherein substituted aryl is defined in K herein;
- (f<sup>1</sup>) carboxylheteroaryl wherein heteroaryl is defined in L herein;
- (g<sup>1</sup>) carboxyl-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (h<sup>1</sup>) carboxylheterocyclic wherein heterocyclic is defined in N herein;
- (i<sup>1</sup>) carboxyl-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (j<sup>1</sup>) cycloalkyl as defined in F herein;
- (k<sup>1</sup>) substituted cycloalkyl as defined in G herein;
- (l<sup>1</sup>) guanidino as defined in C38 herein;
- (m<sup>1</sup>) guanidinosulfone as defined in C39 herein;
- (n<sup>1</sup>) thiol as defined in X<sup>2</sup> herein;
- (o<sup>1</sup>) thioalkyl as defined in X herein;
- (p<sup>1</sup>) substituted thioalkyl as defined in C42 herein;
- (q<sup>1</sup>) thioaryl as defined in C43 herein;
- (r<sup>1</sup>) substituted thioaryl as defined in C44 herein;
- (s<sup>1</sup>) thiocycloalkyl as defined in C45 herein;
- (t<sup>1</sup>) substituted thiocycloalkyl as defined in C46 herein;
- (u<sup>1</sup>) thioheteroaryl as defined in C47 herein;
- (v<sup>1</sup>) substituted thioheteroaryl as defined in C48 herein;
- (w<sup>1</sup>) thioheterocyclic as defined in C49 herein;

- (x<sup>1</sup>) substituted thioheterocyclic as defined in C50 herein;
- (y<sup>1</sup>) heteroaryl as defined in L herein;
- (z<sup>1</sup>) substituted heteroaryl as defined in M herein;
- (a<sup>2</sup>) heterocyclic as defined in N herein;
- (b<sup>2</sup>) substituted heterocyclic as defined in O herein;
- (c<sup>2</sup>) cycloalkoxy as defined in E<sup>1</sup> herein;
- (d<sup>2</sup>) substituted cycloalkoxy as defined in F<sup>1</sup> herein;
- (e<sup>2</sup>) heteroaryloxy as defined in K<sup>1</sup> herein;
- (f<sup>2</sup>) substituted heteroaryloxy as defined in L<sup>1</sup> herein;
- (g<sup>2</sup>) heterocyclyloxy as defined in M<sup>1</sup> herein;
- (h<sup>2</sup>) substituted heterocyclyloxy as defined in N<sup>1</sup> herein;
- (i<sup>2</sup>) oxycarbonylamino as defined in Y<sup>1</sup> herein;
- (j<sup>2</sup>) oxythiocarbonylamino as defined in Z<sup>1</sup> herein;
- (k<sup>2</sup>) -OS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (l<sup>2</sup>) -OS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (m<sup>2</sup>) -OS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (n<sup>2</sup>) -OS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (o<sup>2</sup>) -OS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (p<sup>2</sup>) -OS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (q<sup>2</sup>) -OS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (r<sup>2</sup>) -OS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (s<sup>2</sup>) -OSO<sub>2</sub>-NRR where R is:
  - (a) hydrogen; or

- (b) alkyl as defined in B herein;
- (t<sup>2</sup>) -NRS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (u<sup>2</sup>) -NRS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (v<sup>2</sup>) -NRS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (w<sup>2</sup>) -NRS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (x<sup>2</sup>) -NRS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (y<sup>2</sup>) -NRS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (z<sup>2</sup>) -NRS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (a<sup>3</sup>) -NRS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (b<sup>3</sup>) -NRS(O)<sub>2</sub>-NR-alkyl wherein alkyl is defined in B herein;
- (c<sup>3</sup>) -NRS(O)<sub>2</sub>-NR-substituted alkyl wherein substituted alkyl is defined in C herein;
- (d<sup>3</sup>) -NRS(O)<sub>2</sub>-NR-aryl wherein aryl is defined in J herein;
- (e<sup>3</sup>) -NRS(O)<sub>2</sub>-NR-substituted aryl wherein substituted aryl is defined in K herein;
- (f<sup>3</sup>) -NRS(O)<sub>2</sub>-NR-heteroaryl wherein heteroaryl is defined in L herein;
- (g<sup>3</sup>) -NRS(O)<sub>2</sub>-NR-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (h<sup>3</sup>) -NRS(O)<sub>2</sub>-NR-heterocyclic wherein heterocyclic is defined in N herein;

- (i<sup>3</sup>) -NRS(O)<sub>2</sub>-NR-substituted heterocyclic wherein substituted heterocyclic is defined in O herein and where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;
- (j<sup>3</sup>) mono- and di-alkylamino wherein alkylamino is defined in I<sup>29</sup> herein;
- (k<sup>3</sup>) mono- and di-(substituted alkyl)amino wherein substituted alkyl is defined in C herein and amino is defined in C7 herein;
- (l<sup>3</sup>) mono- and di-arylamino wherein aryl is defined in J herein and amino is defined in C7 herein;
- (m<sup>3</sup>) mono- and di-substituted arylamino wherein substituted aryl is defined in K herein and amino is defined in C7 herein;
- (n<sup>3</sup>) mono- and di-heteroarylamino wherein heteroaryl is defined in L herein and amino is defined in C7 herein;
- (o<sup>3</sup>) mono- and di-substituted heteroarylamino wherein substituted heteroaryl is defined in M herein and amino is defined in C7 herein;
- (p<sup>3</sup>) mono- and di-heterocyclic amino wherein heterocyclic is defined in N herein and amino is defined in C7 herein;
- (q<sup>3</sup>) mono- and di-substituted heterocyclic amino wherein substituted heterocyclic is defined in O herein and amino is defined in C7 herein;
- (r<sup>3</sup>) unsymmetric di-substituted amines having different substituents selected from:
  - (a) alkyl as defined in B herein;



- (b) substituted alkyl as defined in C herein;
- (c) aryl as defined in J herein;
- (d) substituted aryl as defined in K herein;
- (e) heteroaryl as defined in L herein;
- (f) substituted heteroaryl as defined in M herein;
- (g) heterocyclic as defined in N herein; and
- (h) substituted heterocyclic as defined in O herein  
and substituted alkynyl groups having amino  
groups blocked by conventional blocking groups  
such as Boc, Cbz, formyl, and the like or  
alkynyl/substituted alkynyl groups substituted  
with:
  - (i) -SO<sub>2</sub>-alkyl wherein alkyl is defined in B  
herein;
  - (ii) -SO<sub>2</sub>-substituted alkyl wherein  
substituted alkyl is defined in C herein;
  - (iii) -SO<sub>2</sub>-alkenyl wherein alkenyl is defined  
in D herein;
  - (iv) -SO<sub>2</sub>-substituted alkenyl wherein  
substituted alkenyl is defined in E herein;
  - (v) -SO<sub>2</sub>-cycloalkyl wherein cycloalkyl is  
defined in F herein;
  - (vi) -SO<sub>2</sub>-substituted cycloalkyl wherein  
substituted cycloalkyl is defined in G  
herein;
  - (vii) -SO<sub>2</sub>-aryl wherein aryl is defined in J  
herein;
  - (viii) -SO<sub>2</sub>-substituted aryl wherein substituted  
aryl is defined in K herein;

- (ix) -SO<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (x) -SO<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (xi) -SO<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (xii) -SO<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein; and
- (xiii) -SO<sub>2</sub>NRR where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;

- (R<sup>2</sup>) cyano;
- (S<sup>2</sup>) acyl as defined in R<sup>1</sup> herein;
- (T<sup>2</sup>) substituted acyl;
- (U<sup>2</sup>) carboxy;
- (V<sup>2</sup>) substituted carboxy;
- (W<sup>2</sup>) nitro;
- (X<sup>2</sup>) thiol having the formula "-SH";
- (Y<sup>2</sup>) alkylthio as defined in X herein;
- (Z<sup>2</sup>) substituted alkylthio having the formula "-S-substituted alkyl";
- (A<sup>3</sup>) alkylsulfoxy having the formula "-SO-alkyl";
- (B<sup>3</sup>) substituted alkylsulfoxy having the formula "-SO-substituted alkyl";
- (C<sup>3</sup>) alkylsulfonyl having the formula "-SO<sub>2</sub>-alkyl";
- (D<sup>3</sup>) substituted alkylsulfonyl having the formula "-SO<sub>2</sub>-substituted alkyl";
- (E<sup>3</sup>) aryl as defined in J herein;
- (F<sup>3</sup>) substituted aryl as defined in K herein;
- (G<sup>3</sup>) heteroaryl as defined in L herein; and

(H<sup>3</sup>) substituted heteroaryl as defined in M herein;

R<sup>2</sup> is selected from the group consisting of:

(I<sup>3</sup>) alkyl as defined in B herein;

(J<sup>3</sup>) substituted alkyl as defined in C herein;

(K<sup>3</sup>) aryl as defined in J herein;

(L<sup>3</sup>) substituted aryl as defined in K herein;

(M<sup>3</sup>) heteroaryl as defined in L herein;

(N<sup>3</sup>) substituted heteroaryl as defined in M herein;

(O<sup>3</sup>) cycloalkyl as defined in F herein;

(P<sup>3</sup>) substituted cycloalkyl as defined in G herein;

(Q<sup>3</sup>) cycloalkenyl as defined in H herein; and

(R<sup>3</sup>) substituted cycloalkenyl as defined in I herein;

C is a group wherein W', together with -C(=Z)N-, forms a saturated or unsaturated heterocyclic group containing 2 to 5 carbon atoms and 0 to 4 additional heteroatoms selected from the group consisting of:

(S<sup>3</sup>) nitrogen;

(T<sup>3</sup>) oxygen; and

(U<sup>3</sup>) -So<sub>n</sub>- (where n is 0 to 2);

wherein said saturated or unsaturated heterocyclic group is optionally fused with one or two ring(s) structures selected from the group consisting of:

(V<sup>3</sup>) cycloalkyl as defined in F herein;

(W<sup>3</sup>) cycloalkenyl as defined in H herein;

(X<sup>3</sup>) heterocyclic as defined in N herein;

(Y<sup>3</sup>) aryl as defined in J herein; and

(Z<sup>3</sup>) heteroaryl group, wherein heteroaryl is defined in L herein, to form a bi- or tri-fused ring system and further wherein said heterocyclic group and each of such ring structures are optionally substituted with 1 to 3 substituents selected from the group consisting of with one or two substituent(s) selected from the group consisting of:

- (1) hydrogen;
- (2) halogen as defined in Q herein;
- (3) hydroxy;
- (4) alkoxy as defined in V herein;
- (5) substituted alkoxy as defined in B<sup>1</sup> herein;
- (6) alkylenedioxy;
- (7) acyloxy as defined in T<sup>1</sup> herein;
- (8) substituted acyloxy;
- (9) amino as defined in C7 herein;
- (10) alkylamino as defined in I<sup>2</sup>9 herein;
- (11) substituted alkylamino as defined in I<sup>2</sup>10 herein;
- (12) dialkylamino as defined in I<sup>2</sup>11 herein;
- (13) substituted dialkylamino as defined in I<sup>2</sup>12 herein;
- (14) acylamino as defined in S<sup>1</sup> herein;
- (15) substituted acylamino;
- (16) N-acyl-N-alkylamino wherein acyl is defined in R<sup>1</sup> herein and alkylamino I<sup>2</sup>9 herein;
- (17) substituted N-acyl-N-alkylamino wherein acyl is defined in R<sup>1</sup> herein and substituted alkylamino is defined in I<sup>2</sup>10 herein;
- (18) (alkylsulfonyl)amino wherein alkylsulfonyl is defined in C<sup>3</sup> herein and amino is defined in C7 herein;
- (19) substituted (alkylsulfonyl)amino wherein substituted alkylsulfonyl is defined in D<sup>3</sup> herein and amino is defined in C7 herein;
- (20) N-(alkylsulfonyl)-N-alkylamino wherein alkylsulfonyl is defined in C<sup>3</sup> herein and alkylamino is defined in I<sup>2</sup>9 herein;
- (21) substituted N-(alkylsulfonyl)-N-alkylamino wherein substituted alkylsulfonyl is defined in D<sup>3</sup> herein and substituted alkylamino is defined in I<sup>2</sup>10 herein;

- (22) alkyl as defined in B herein;
- (23) substituted alkyl as defined in C herein;
- (24) cycloalkyl as defined in F herein;
- (25) substituted cycloalkyl as defined in G herein;
- (26) alkenyl as defined in D herein;
- (27) substituted alkenyl as defined in E herein;
- (28) cycloalkenyl as defined in H herein;
- (29) substituted cycloalkenyl as defined in I herein;
- (30) alkynyl as defined in U herein;
- (31) substituted alkynyl as defined in Q<sup>231</sup> herein;
- (32) cyano;
- (33) nitro;
- (34) acyl as defined in R<sup>1</sup> herein;
- (35) substituted acyl;
- (36) carboxy;
- (37) substituted carboxy;
- (38) thiol as defined in X<sup>2</sup> herein;
- (39) alkylthio as defined in X herein;
- (40) substituted alkylthio as defined in Z<sup>2</sup> herein;
- (41) alkylsulfoxy as defined in A<sup>3</sup> herein;
- (42) substituted alkylsulfoxy as defined in B<sup>3</sup> herein;
- (43) alkylsulfonyl as defined in C<sup>3</sup> herein;
- (44) substituted alkylsulfonyl as defined in D<sup>3</sup> herein;
- (45) aryl as defined in J herein;
- (46) substituted aryl as defined in K herein;
- (47) heteroaryl as defined in L herein; and
- (48) substituted heteroaryl as defined in M herein; or

(iii) HetAr where HetAr is a:

(A<sup>4</sup>) nitrogen containing heteroaryl, having a heteroaryl ring that contains at least one nitrogen atom in the ring, and that is optionally substituted with:

- (1) aryl as defined in J herein; or
- (2) substituted aryl group, wherein substituted aryl is defined in K herein;

or enantiomers, diastereomers or pharmaceutically acceptable salts thereof;  
and further wherein the compound of Formula I has a binding affinity to VLA-4 as expressed by an IC<sub>50</sub> of about 15  $\mu$ M or less.

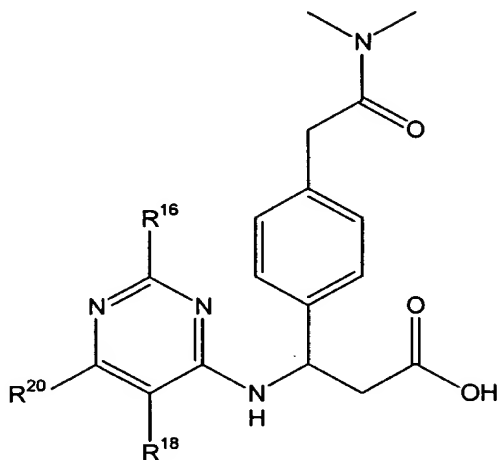
48. (Amended) A method for treating a disease mediated by VLA-4 in a patient, wherein the disease is selected from the group consisting of asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, acute juvenile onset diabetes, inflammatory bowel disease, ulcerative colitis, Crohn's disease, multiple sclerosis, rheumatoid arthritis, tissue transplantation, tumor metastasis, meningitis, encephalitis, stroke, and other cerebral traumas, nephritis, retinitis, atopic dermatitis, psoriasis, myocardial ischemia, acute leukocyte-mediated lung injury, adult respiratory distress syndrome, erythema nodosum, allergic conjunctivitis, optic neuritis, uveitis, allergic rhinitis, Ankylosing spondylitis, psoriatic arthritis, vasculitis, Reiter's syndrome, systemic lupus erythematosus, progressive systemic sclerosis, polymyositis, dermatomyositis, Wegner's granulomatosis, aortitis, sarcoidosis, lymphocytopenia, temporal arteritis, pericarditis, myocarditis, congestive heart failure, polyarteritis nodosa, hypersensitivity syndromes, allergy, hypereosinophilic syndromes, Churg-Strauss syndrome, chronic obstructive pulmonary disease, hypersensitivity pneumonitis, chronic active hepatitis, interstitial cystitis, autoimmune endocrine failure, primary biliary cirrhosis, autoimmune aplastic anemia, chronic persistent hepatitis and thyroiditis, which method comprises administering a pharmaceutical

composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of any one of Claims 27-32 or 34-47.

50. (Amended) A method for treating a disease mediated by VLA-4 in a patient, wherein the disease is selected from the group consisting of asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, acute juvenile onset diabetes, inflammatory bowel disease, ulcerative colitis, Crohn's disease, multiple sclerosis, rheumatoid arthritis, tissue transplantation, tumor metastasis, meningitis, encephalitis, stroke, and other cerebral traumas, nephritis, retinitis, atopic dermatitis, psoriasis, myocardial ischemia, acute leukocyte-mediated lung injury, adult respiratory distress syndrome, erythema nodosum, allergic conjunctivitis, optic neuritis, uveitis, allergic rhinitis, Ankylosing spondylitis, psoriatic arthritis, vasculitis, Reiter's syndrome, systemic lupus erythematosus, progressive systemic sclerosis, polymyositis, dermatomyositis, Wegner's granulomatosis, aortitis, sarcoidosis, lymphocytopenia, temporal arteritis, pericarditis, myocarditis, congestive heart failure, polyarteritis nodosa, hypersensitivity syndromes, allergy, hypereosinophilic syndromes, Churg-Strauss syndrome, chronic obstructive pulmonary disease, hypersensitivity pneumonitis, chronic active hepatitis, interstitial cystitis, autoimmune endocrine failure, primary biliary cirrhosis, autoimmune aplastic anemia, chronic persistent hepatitis and thyroiditis, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 33.

Please add the following new claims 53-56.

53. (New) A compound having the structure



wherein:

R<sup>16</sup> is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

R<sup>18</sup> is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic; and

R<sup>20</sup> is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen.



54. (New) A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 53.

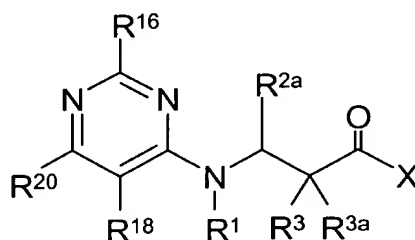
55. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 53.

56. (New) A method for binding VLA-4 in a biological sample which method comprises contacting the biological sample, comprising blood or plasma withdrawn from a patient, with a compound of Claim 53 under conditions wherein said compound binds to VLA-4.

## APPENDIX B

### PENDING CLAIMS AFTER AMENDMENT HEREIN

27. A compound of Formula (I):



(I)

wherein:

R<sup>1</sup> is selected from the group consisting of:

- A) hydrogen;
- B) alkyl of from 1 to 6 carbon atoms;
- C) substituted alkyl of from 1 to 10 carbon atoms, having 1 to 5 substituents selected from the group consisting of:
  - (1) alkoxy as defined in V herein;
  - (2) substituted alkoxy as defined in B<sup>1</sup> herein;
  - (3) acyl as defined in R<sup>1</sup> herein;
  - (4) acylamino as defined in S<sup>1</sup> herein;
  - (5) thiocarbonylamino as defined in B<sup>2</sup> herein;
  - (6) acyloxy as defined in T<sup>1</sup> herein;
  - (7) amino having the formula "-NH<sub>2</sub>-";
  - (8) amidino having the formula "H<sub>2</sub>NC(=NH)-";
  - (9) alkyl amidino wherein alkyl is defined in B herein and amidino is defined in C8 herein;
  - (10) thioamidino as defined in A<sup>2</sup> herein;
  - (11) aminoacyl as defined in U<sup>1</sup> herein;

- (12) aminocarbonylamino as defined in V<sup>1</sup> herein;
- (13) aminothiocabonylamino as defined in W<sup>1</sup> herein;
- (14) aminocarbonyloxy as defined in X<sup>1</sup> herein;
- (15) aryl as defined in J herein;
- (16) substituted aryl as defined in K herein;
- (17) aryloxy as defined in I<sup>1</sup> herein;
- (18) substituted aryloxy as defined in J<sup>1</sup> herein;
- (19) aryloxyaryl having the formula "aryl-O-aryl";
- (20) substituted aryloxyaryl having the formula "aryl-O-aryl"  
substituted with from 1 to 3 substituents on either or both aryl  
rings selected from the group consisting of:
  - (a) hydroxy;
  - (b) acyl as defined in R<sup>1</sup> herein;
  - (c) acylamino as defined in S<sup>1</sup> herein;
  - (d) thiocarbonylamino as defined in B<sup>2</sup> herein;
  - (e) acyloxy as defined in T<sup>1</sup> herein;
  - (f) alkyl as defined in B herein;
  - (g) substituted alkyl as defined in C herein;
  - (h) alkoxy as defined in V herein;
  - (i) substituted alkoxy as defined in B<sup>1</sup> herein;
  - (j) alkenyl as defined in D herein;
  - (k) substituted alkenyl as defined in E herein;
  - (l) alkynyl as defined in U herein;
  - (m) substituted alkynyl as defined in Q<sup>231</sup> herein;
  - (n) amidino as defined in C8 herein;
  - (o) alkylamidino wherein alkyl is defined in B herein and  
amidino is defined in C8 herein;
  - (p) thioamidino as defined in A<sup>2</sup> herein;

- (q) amino as defined in C7 herein;
- (r) aminoacyl as defined in U<sup>1</sup> herein;
- (s) aminocarbonyloxy as defined in X<sup>1</sup> herein;
- (t) aminocarbonylamino as defined in V<sup>1</sup> herein;
- (u) aminothiocabonylamino as defined in W<sup>1</sup> herein;
- (v) aryl as defined in J herein;
- (w) substituted aryl as defined in K herein;
- (x) aryloxy as defined in I<sup>1</sup> herein;
- (y) substituted aryloxy as defined in J<sup>1</sup> herein;
- (z) cycloalkoxy as defined in E<sup>1</sup> herein;
- (a<sup>1</sup>) substituted cycloalkoxy as defined in F<sup>1</sup> herein;
- (b<sup>1</sup>) heteroaryloxy as defined in K<sup>1</sup> herein;
- (c<sup>1</sup>) substituted heteroaryloxy as defined in L<sup>1</sup> herein;
- (d<sup>1</sup>) heterocyclyloxy as defined in M<sup>1</sup> herein;
- (e<sup>1</sup>) substituted heterocyclyloxy as defined in N<sup>1</sup> herein;
- (f<sup>1</sup>) carboxyl;
- (g<sup>1</sup>) carboxylalkyl wherein alkyl is defined in B herein;
- (h<sup>1</sup>) carboxyl-substituted alkyl wherein substituted alkyl is defined in C herein;
- (i<sup>1</sup>) carboxyl-cycloalkyl wherein cycloalkyl is defined in F herein;
- (j<sup>1</sup>) carboxyl-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
- (k<sup>1</sup>) carboxylaryl wherein aryl is defined in J herein;
- (l<sup>1</sup>) carboxyl-substituted aryl wherein substituted aryl is defined in K herein;
- (m<sup>1</sup>) carboxylheteroaryl wherein heteroaryl is defined in L herein;

- (n<sup>1</sup>) carboxyl-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (o<sup>1</sup>) carboxylheterocyclic wherein heterocyclic is defined in N herein;
- (p<sup>1</sup>) carboxyl-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (q<sup>1</sup>) carboxylamido;
- (r<sup>1</sup>) cyano;
- (s<sup>1</sup>) thiol as defined in X<sup>2</sup> herein;
- (t<sup>1</sup>) thioalkyl as defined in X herein;
- (u<sup>1</sup>) substituted thioalkyl as defined in C42 herein;
- (v<sup>1</sup>) thioaryl as defined in C43 herein;
- (w<sup>1</sup>) substituted thioaryl as defined in C44 herein;
- (x<sup>1</sup>) thioheteroaryl as defined in C47 herein;
- (y<sup>1</sup>) substituted thioheteroaryl as defined in C48 herein;
- (z<sup>1</sup>) thiocycloalkyl as defined in C45 herein;
- (a<sup>2</sup>) substituted thiocycloalkyl as defined in C46 herein;
- (b<sup>2</sup>) thioheterocyclic as defined in C49 herein;
- (c<sup>2</sup>) substituted thioheterocyclic as defined in C50 herein;
- (d<sup>2</sup>) cycloalkyl as defined in F herein;
- (e<sup>2</sup>) substituted cycloalkyl as defined in G herein;
- (f<sup>2</sup>) guanidino as defined in C38 herein;
- (g<sup>2</sup>) guanidinosulfone as defined in C39 herein;
- (h<sup>2</sup>) halo as defined in Q herein;
- (i<sup>2</sup>) nitro;
- (j<sup>2</sup>) heteroaryl as defined in L herein;
- (k<sup>2</sup>) substituted heteroaryl as defined in M herein;
- (l<sup>2</sup>) heterocyclic as defined in N herein;

- (m<sup>2</sup>) substituted heterocyclic as defined in O herein;
- (n<sup>2</sup>) cycloalkoxy as defined in E<sup>1</sup> herein;
- (o<sup>2</sup>) substituted cycloalkoxy as defined in F<sup>1</sup> herein;
- (p<sup>2</sup>) heteroaryloxy as defined in K<sup>1</sup> herein;
- (q<sup>2</sup>) substituted heteroaryloxy as defined in L<sup>1</sup> herein;
- (r<sup>2</sup>) heterocyclyloxy as defined in M<sup>1</sup> herein;
- (s<sup>2</sup>) substituted heterocyclyloxy as defined in N<sup>1</sup> herein;
- (t<sup>2</sup>) oxycarbonylamino as defined in Y<sup>1</sup> herein;
- (u<sup>2</sup>) oxythiocarbonylamino as defined in Z<sup>1</sup> herein;
- (v<sup>2</sup>) -S(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (w<sup>2</sup>) -S(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (x<sup>2</sup>) -S(O)<sub>2</sub>-cycloalkyl wherein cycloalkyl is defined in F herein;
- (y<sup>2</sup>) -S(O)<sub>2</sub>-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
- (z<sup>2</sup>) -S(O)<sub>2</sub>-alkenyl wherein alkenyl is defined in D herein;
- (a<sup>3</sup>) -S(O)<sub>2</sub>-substituted alkenyl wherein substituted alkenyl is defined in E herein;
- (b<sup>3</sup>) -S(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (c<sup>3</sup>) -S(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (d<sup>3</sup>) -S(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (e<sup>3</sup>) -S(O)<sub>2</sub>-substituted heteroaryl wherein substituted aryl is defined in M herein;
- (f<sup>3</sup>) -S(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;

- (g<sup>3</sup>) -S(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (h<sup>3</sup>) -OS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (i<sup>3</sup>) -OS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (j<sup>3</sup>) -OS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (k<sup>3</sup>) -OS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (l<sup>3</sup>) -OS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (m<sup>3</sup>) -OS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (n<sup>3</sup>) -OS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (o<sup>3</sup>) -OS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (p<sup>3</sup>) -OSO<sub>2</sub>-NRR where R is:
  - (i) hydrogen; or
  - (ii) alkyl as defined in B herein;
- (q<sup>3</sup>) -NRS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (r<sup>3</sup>) -NRS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (s<sup>3</sup>) -NRS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (t<sup>3</sup>) -NRS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (u<sup>3</sup>) -NRS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;

- (v<sup>3</sup>) -NRS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (w<sup>3</sup>) -NRS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (x<sup>3</sup>) -NRS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (y<sup>3</sup>) -NRS(O)<sub>2</sub>-NR-alkyl wherein alkyl is defined in B herein;
- (z<sup>3</sup>) -NRS(O)<sub>2</sub>-NR-substituted alkyl wherein substituted alkyl is defined in C herein;
- (a<sup>4</sup>) -NRS(O)<sub>2</sub>-NR-aryl wherein aryl is defined in J herein;
- (b<sup>4</sup>) -NRS(O)<sub>2</sub>-NR-substituted aryl wherein substituted aryl is defined in K herein;
- (c<sup>4</sup>) -NRS(O)<sub>2</sub>-NR-heteroaryl wherein heteroaryl is defined in L herein;
- (d<sup>4</sup>) -NRS(O)<sub>2</sub>-NR-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (e<sup>4</sup>) -NRS(O)<sub>2</sub>-NR-heterocyclic wherein heterocyclic is defined in N herein;
- (f<sup>4</sup>) -NRS(O)<sub>2</sub>-NR-substituted heterocyclic wherein substituted heterocyclic is defined in O herein and where R is:
  - (i) hydrogen; or
  - (ii) alkyl as defined in B herein;
- (g<sup>4</sup>) mono- and di-alkylamino wherein alkylamino is defined in I<sup>29</sup> herein;
- (h<sup>4</sup>) mono- and di-(substituted alkyl)amino wherein substituted alkylamino is defined in I<sup>210</sup> herein;



- (i<sup>4</sup>) mono- and di-arylamino wherein aryl is defined in J herein and amino is defined in C7 herein;
- (j<sup>4</sup>) mono- and di-substituted arylamino wherein substituted aryl is defined in K herein and amino is defined in C7 herein;
- (k<sup>4</sup>) mono- and di-heteroarylamino wherein heteroaryl is defined in L herein and amino is defined in C7 herein;
- (l<sup>4</sup>) mono- and di-substituted heteroarylamino wherein substituted heteroaryl is defined in M herein and amino is defined in C7 herein;
- (m<sup>4</sup>) mono- and di-heterocyclic amino wherein heterocyclic is defined in N herein and amino is defined in C7 herein;
- (n<sup>4</sup>) mono- and di-substituted heterocyclic amino wherein substituted heterocyclic is defined in O herein and amino is defined in C7 herein;
- (o<sup>4</sup>) unsymmetric di-substituted amines having different substituents selected from:
  - (i) alkyl as defined in B herein;
  - (ii) substituted alkyl as defined in C herein;
  - (iii) aryl as defined in J herein;
  - (iv) substituted aryl as defined in K herein;
  - (v) heteroaryl as defined in L herein;
  - (vi) substituted heteroaryl as defined in M herein;
  - (vii) heterocyclic as defined in N herein;
  - (viii) substituted heterocyclic as defined in O herein;and

(ix) amino groups, as defined in C7 herein, on the substituted aryl blocked by conventional blocking groups such as Boc, Cbz, formyl, and the like or substituted with -SO<sub>2</sub>NRR where R is:

(a) hydrogen; or

(b) alkyl as defined in B herein;

- (21) cyano;
- (22) halogen as defined in Q herein;
- (23) hydroxyl;
- (24) nitro;
- (25) carboxyl;
- (26) carboxylalkyl wherein alkyl is defined in B herein;
- (27) carboxyl-substituted alkyl wherein substituted alkyl is defined in C herein;
- (28) carboxyl-cycloalkyl wherein cycloalkyl is defined in F herein;
- (29) carboxyl-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
- (30) carboxylaryl wherein aryl is defined in J herein;
- (31) carboxyl-substituted aryl wherein substituted aryl is defined in K herein;
- (32) carboxylheteroaryl wherein heteroaryl is defined in L herein;
- (33) carboxyl-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (34) carboxylheterocyclic wherein heterocyclic is defined in N herein;
- (35) carboxyl-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;

- (36) cycloalkyl as defined in F herein;
- (37) substituted cycloalkyl as defined in G herein;
- (38) guanidino having the formula -NRC(=NR)NRR, -  
NRC(=NR)NR-alkyl, -NRC(=NR)NR-substituted alkyl, -  
NRC(=NR)NR-alkenyl, -NRC(=NR)NR-substituted alkenyl, -  
NRC(=NR)NR-alkynyl, -NRC(=NR)NR-substituted alkynyl, -  
NRC(=NR)NR-aryl, -NRC(=NR)NR-substituted aryl, -  
NRC(=NR)NR-cycloalkyl, -NRC(=NR)NR-heteroaryl, -  
NRC(=NR)NR-substituted heteroaryl, -NRC(=NR)NR-  
heterocyclic, and -NRC(=NR)NR-substituted heterocyclic  
where each R is independently hydrogen and alkyl as well as  
where one of the amino groups is blocked by conventional  
blocking groups such as Boc, Cbz, formyl, and the like and  
wherein alkyl is defined in B herein; substituted alkyl is defined  
in C herein; alkenyl is defined in D herein; substituted alkenyl  
is defined in E herein; alkynyl is defined in U herein;  
substituted alkynyl is defined in Q<sup>231</sup> herein; cycloalkyl is  
defined in F herein; substituted cycloalkyl is defined in G  
herein; aryl is defined in J herein; substituted aryl is defined in  
K herein; heteroaryl is defined in L herein; substituted  
heteroaryl is defined in M herein; heterocyclic is defined in N  
herein; and substituted heterocyclic is defined in O herein;
- (39) guanidinosulfone having the formula -NRC(=NR)NRSO<sub>2</sub>-alkyl,  
-NRC(=NR)NRSO<sub>2</sub>-substituted alkyl, -NRC(=NR)NRSO<sub>2</sub>-  
alkenyl, -NRC(=NR)NRSO<sub>2</sub>-substituted alkenyl, -  
NRC(=NR)NRSO<sub>2</sub>-alkynyl, -NRC(=NR)NRSO<sub>2</sub>-substituted  
alkynyl, -NRC(=NR)NRSO<sub>2</sub>-aryl, -NRC(=NR)NRSO<sub>2</sub>-  
substituted aryl, -NRC(=NR)NRSO<sub>2</sub>-cycloalkyl, -

NRC(=NR)NRSO<sub>2</sub>-substituted cycloalkyl, -NRC(=NR)NRSO<sub>2</sub>-heteroaryl, and -NRC(=NR)NRSO<sub>2</sub>-substituted heteroaryl, -NRC(=NR)NRSO<sub>2</sub>-heterocyclic, and -NRC(=NR)NRSO<sub>2</sub>-substituted heterocyclic where each R is independently hydrogen and alkyl and wherein alkyl is defined in B herein; substituted alkyl is defined in C herein; alkenyl is defined in D herein; substituted alkenyl is defined in E herein; alkynyl is defined in U herein; substituted alkynyl is defined in Q<sup>231</sup> herein; cycloalkyl is defined in F herein; substituted cycloalkyl is defined in G herein; aryl is defined in J herein; substituted aryl is defined in K herein; heteroaryl is defined in L herein; substituted heteroaryl is defined in M herein; heterocyclic is defined in N herein; and substituted heterocyclic is defined in O herein;

- (40) thiol as defined in X<sup>2</sup> herein;
- (41) thioalkyl as defined in X herein;
- (42) substituted thioalkyl having the formula "-S-substituted alkyl";
- (43) thioaryl having the formula "-S-aryl";
- (44) substituted thioaryl having the formula "-S-substituted aryl";
- (45) thiocycloalkyl having the formula "-S-cycloalkyl";
- (46) substituted thiocycloalkyl having the formula "-S-substituted cycloalkyl";
- (47) thioheteroaryl having the formula "-S-heteroaryl";
- (48) substituted thioheteroaryl having the formula "-s-substituted heteroaryl";
- (49) thioheterocyclic having the formula "-S-heterocyclic";
- (50) substituted thioheterocyclic having the formula "-S-substituted heterocyclic";

- (51) heteroaryl as defined in L herein;
- (52) substituted heteroaryl as defined in M herein;
- (53) heterocyclic as defined in N herein;
- (54) substituted heterocyclic as defined in O herein;
- (55) cycloalkoxy as defined in E<sup>1</sup> herein;
- (56) substituted cycloalkoxy as defined in F<sup>1</sup> herein;
- (57) heteroaryloxy as defined in K<sup>1</sup> herein;
- (58) substituted heteroaryloxy as defined in L<sup>1</sup> herein;
- (59) heterocyclyloxy as defined in M<sup>1</sup> herein;
- (60) substituted heterocyclyloxy as defined in N<sup>1</sup> herein;
- (61) oxycarbonylamino as defined in Y<sup>1</sup> herein;
- (62) oxythiocarbonylamino as defined in Z<sup>1</sup> herein;
- (63) -OS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (64) -OS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (65) -OS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (66) -OS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (67) -OS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (68) -OS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (69) -OS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (70) -OS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (71) -OSO<sub>2</sub>-NRR where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;

- (72) -NRS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (73) -NRS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (74) -NRS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (75) -NRS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (76) -NRS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (77) -NRS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (78) -NRS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (79) -NRS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (80) -NRS(O)<sub>2</sub>-NR-alkyl wherein alkyl is defined in B herein;
- (81) -NRS(O)<sub>2</sub>-NR-substituted alkyl wherein substituted alkyl is defined in C herein;
- (82) -NRS(O)<sub>2</sub>-NR-aryl wherein aryl is defined in J herein;
- (83) -NRS(O)<sub>2</sub>-NR-substituted aryl wherein substituted aryl is defined in K herein;
- (84) -NRS(O)<sub>2</sub>-NR-heteroaryl wherein heteroaryl is defined in L herein;
- (85) -NRS(O)<sub>2</sub>-NR-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (86) -NRS(O)<sub>2</sub>-NR-heterocyclic wherein heterocyclic is defined in N herein;
- (87) -NRS(O)<sub>2</sub>-NR-substituted heterocyclic wherein substituted heterocyclic is defined as O herein and where R is:
  - (a) hydrogen; or

- (b) alkyl as defined in B herein;
- (88) mono- and di-alkylamino wherein alkylamino is defined in I<sup>2</sup>9 herein;
- (89) mono- and di-(substituted alkyl)amino wherein substituted alkylamino is defined in I<sup>2</sup>10 herein;
- (90) mono- and di-arylamino wherein aryl is defined in J herein and amino is defined in C7 herein;
- (91) mono- and di-substituted arylamino wherein substituted aryl is defined in K herein and amino is defined in C7 herein;
- (92) mono- and di-heteroarylamino wherein heteroaryl is defined in L herein and amino is defined in C7 herein;
- (93) mono- and di-substituted heteroarylamino wherein substituted heteroaryl is defined in M herein and amino is defined in C7 herein;
- (94) mono- and di-heterocyclic amino wherein heterocyclic is defined in N herein and amino is defined in C7 herein;
- (95) mono- and di-substituted heterocyclic amino wherein substituted heterocyclic is defined in O herein and amino is defined in C7 herein;
- (96) unsymmetric di-substituted amines having different substituents selected from:
  - (a) alkyl as defined in B herein;
  - (b) substituted alkyl as defined in C herein;
  - (c) aryl as defined in J herein;
  - (d) substituted aryl as defined in K herein;
  - (e) heteroaryl as defined in L herein;
  - (f) substituted heteroaryl as defined in M herein;
  - (g) heterocyclic as defined in N herein;

- (h) substituted heterocyclic as defined in O herein; and
- (i) substituted alkyl groups having amino groups blocked by conventional blocking groups such as Boc, Cbz, formyl, and the like or alkyl/substituted alkyl groups substituted with:
  - (i) -SO<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
  - (ii) -SO<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
  - (iii) -SO<sub>2</sub>-alkenyl wherein alkenyl is defined in D herein;
  - (iv) -SO<sub>2</sub>-substituted alkenyl wherein substituted alkenyl is defined in E herein;
  - (v) -SO<sub>2</sub>-cycloalkyl wherein cycloalkyl is defined in F herein;
  - (vi) -SO<sub>2</sub>-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
  - (vii) -SO<sub>2</sub>-aryl wherein aryl is defined in J herein;
  - (viii) -SO<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
  - (ix) -SO<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
  - (x) -SO<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
  - (xi) -SO<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
  - (xii) -SO<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- and



(xiii) -SO<sub>2</sub>NRR where R is:

(a) hydrogen; or

(b) alkyl as defined in B herein;

- D) alkenyl of from 2 to 6 carbon atoms and from 1-2 sites of alkenyl unsaturation;
- E) substituted alkenyl of from 1 to 5 substituents selected from the group consisting of:
- (1) alkoxy as defined in V herein;
  - (2) substituted alkoxy as defined in B<sup>1</sup> herein;
  - (3) acyl as defined in R<sup>1</sup> herein;
  - (4) acylamino as defined in S<sup>1</sup> herein;
  - (5) thiocarbonylamino as defined in B<sup>2</sup> herein;
  - (6) acyloxy as defined in T<sup>1</sup> herein;
  - (7) amino as defined in C7 herein;
  - (8) amidino as defined in C8 herein;
  - (9) alkylamidino wherein alkyl is defined in B herein and amidino is defined in C8 herein;
  - (10) thioamidino as defined in A<sup>2</sup> herein;
  - (11) aminoacyl as defined in U<sup>1</sup> herein;
  - (12) aminocarbonylamino as defined in V<sup>1</sup> herein;
  - (13) aminothiocarbonylamino as defined in W<sup>1</sup> herein;
  - (14) aminocarbonyloxy as defined in X<sup>1</sup> herein;
  - (15) aryl as defined in J herein;
  - (16) substituted aryl as defined in K herein;
  - (17) aryloxy as defined in I<sup>1</sup> herein;
  - (18) substituted aryloxy as defined in J<sup>1</sup> herein;
  - (19) aryloxyaryl as defined in C19 herein;
  - (20) substituted aryloxyaryl as defined in C20 herein;

- (21) halogen as defined in Q herein;
- (22) hydroxyl;
- (23) cyano;
- (24) nitro;
- (25) carboxyl;
- (26) carboxylalkyl wherein alkyl is defined in B herein;
- (27) carboxyl-substituted alkyl wherein substituted alkyl is defined in C herein;
- (28) carboxyl-cycloalkyl wherein cycloalkyl is defined in F herein;
- (29) carboxyl-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
- (30) carboxylaryl wherein aryl is defined in J herein;
- (31) carboxyl-substituted aryl wherein substituted aryl is defined in K herein;
- (32) carboxylheteroaryl wherein heteroaryl is defined in L herein;
- (33) carboxyl-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (34) carboxylheterocyclic wherein heterocyclic is defined in N herein;
- (35) carboxyl-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (36) cycloalkyl as defined in F herein;
- (37) substituted cycloalkyl as defined in G herein;
- (38) guanidino as defined in C38 herein;
- (39) guanidiniosulfone as defined in C39 herein;
- (40) thiol as defined in X<sup>2</sup> herein;
- (41) thioalkyl as defined in X herein;
- (42) substituted thioalkyl as defined in C42 herein;

- (43) thioaryl as defined in C43 herein;
- (44) substituted thioaryl as defined in C44 herein;
- (45) thiocycloalkyl as defined in C45 herein;
- (46) substituted thiocycloalkyl as defined in C46 herein;
- (47) thioheteroaryl as defined in C47 herein;
- (48) substituted thioheteroaryl as defined in C48 herein;
- (49) thioheterocyclic as defined in C49 herein;
- (50) substituted thioheterocyclic as defined in C50 herein;
- (51) heteroaryl as defined in L herein;
- (52) substituted heteroaryl as defined in M herein;
- (53) heterocyclic as defined in N herein;
- (54) substituted heterocyclic as defined in O herein;
- (55) cycloalkoxy as defined in E<sup>1</sup> herein;
- (56) substituted cycloalkoxy as defined in F<sup>1</sup> herein;
- (57) heteroaryloxy as defined in K<sup>1</sup> herein;
- (58) substituted heteroaryloxy as defined in L<sup>1</sup> herein;
- (59) heterocyclyloxy as defined in M<sup>1</sup> herein;
- (60) substituted heterocyclyloxy as defined in N<sup>1</sup> herein;
- (61) oxycarbonylamino as defined in Y<sup>1</sup> herein;
- (62) oxythiocarbonylamino as defined in Z<sup>1</sup> herein;
- (63) -OS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (64) -OS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (65) -OS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (66) -OS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (67) -OS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;

- (68)  $-\text{OS}(\text{O})_2$ -substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (69)  $-\text{OS}(\text{O})_2$ -heterocyclic wherein heterocyclic is defined in N herein;
- (70)  $-\text{OS}(\text{O})_2$ -substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (71)  $\text{OSO}_2$ -NRR where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;
- (72)  $-\text{NRS}(\text{O})_2$ -alkyl wherein alkyl is defined in B herein;
- (73)  $-\text{NRS}(\text{O})_2$ -substituted alkyl wherein substituted alkyl is defined in C herein;
- (74)  $-\text{NRS}(\text{O})_2$ -aryl wherein aryl is defined in J herein;
- (75)  $-\text{NRS}(\text{O})_2$ -substituted aryl wherein substituted aryl is defined in K herein;
- (76)  $-\text{NRS}(\text{O})_2$ -heteroaryl wherein heteroaryl is defined in L herein;
- (77)  $-\text{NRS}(\text{O})_2$ -substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (78)  $-\text{NRS}(\text{O})_2$ -heterocyclic wherein heterocyclic is defined in N herein;
- (79)  $-\text{NRS}(\text{O})_2$ -substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (80)  $-\text{NRS}(\text{O})_2$ -NR-alkyl wherein alkyl is defined in B herein;
- (81)  $-\text{NRS}(\text{O})_2$ -NR-substituted alkyl wherein substituted alkyl is defined in C herein;
- (82)  $-\text{NRS}(\text{O})_2$ -NR-aryl wherein aryl is defined in J herein;
- (83)  $-\text{NRS}(\text{O})_2$ -NR-substituted aryl wherein substituted aryl is defined in K herein;

- (84) -NRS(O)<sub>2</sub>-NR-heteroaryl wherein heteroaryl is defined in L herein;
- (85) -NRS(O)<sub>2</sub>-NR-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (86) -NRS(O)<sub>2</sub>-NR-heterocyclic wherein heterocyclic is defined in N herein;
- (87) -NRS(O)<sub>2</sub>-NR-substituted heterocyclic wherein substituted heterocyclic is defined in O herein and where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;
- (88) mono- and di-alkylamino wherein alkylamino is defined in I<sup>29</sup> herein;
- (89) mono- and di-(substituted alkyl)amino wherein substituted alkylamino is defined in I<sup>210</sup> herein;
- (90) mono- and di-arylamino wherein aryl is defined in J herein and amino is defined in C7 herein;
- (91) mono- and di-substituted arylamino wherein substituted aryl is defined in K herein and amino is defined in C7 herein;
- (92) mono- and di-heteroarylamino wherein heteroaryl is defined in L herein and amino is defined in C7 herein;
- (93) mono- and di-substituted heteroarylamino wherein substituted heteroaryl is defined in M herein and amino is defined in C7 herein;
- (94) mono- and di-heterocyclic amino wherein heterocyclic is defined in N herein and amino is defined in C7 herein;
- (95) mono- and di-substituted heterocyclic amino wherein substituted heterocyclic is defined in O herein and amino is defined in C7 herein;

- (96) unsymmetric di-substituted amines having different substituents selected from:
- (a) alkyl as defined in B herein;
  - (b) substituted alkyl as defined in C herein;
  - (c) aryl as defined in J herein;
  - (d) substituted aryl as defined in K herein;
  - (e) heteroaryl as defined in L herein;
  - (f) substituted heteroaryl as defined in M herein;
  - (g) heterocyclic as defined in N herein;
  - (h) substituted heterocyclic as defined in O herein; and
  - (i) substituted alkenyl groups having amino groups blocked by conventional blocking groups such as Boc, Cbz, formyl, and the like or alkenyl/substituted alkenyl groups substituted with:
    - (i) -SO<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
    - (ii) -SO<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
    - (iii) -SO<sub>2</sub>-alkenyl wherein alkenyl is defined in D herein;
    - (iv) -SO<sub>2</sub>-substituted alkenyl wherein substituted alkenyl is defined in E herein;
    - (v) -SO<sub>2</sub>-cycloalkyl wherein cycloalkyl is defined in F herein;
    - (vi) -SO<sub>2</sub>-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
    - (vii) -SO<sub>2</sub>-aryl wherein aryl is defined in J herein;

- (viii) -SO<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
  - (ix) -SO<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
  - (x) -SO<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
  - (xi) -SO<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
  - (xii) -SO<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein; and
  - (xiii) -SO<sub>2</sub>NRR where R is:
    - (a) hydrogen; or
    - (b) alkyl as defined in B herein;
- F) cycloalkyl of from 3 to 8 carbon atoms;
- G) substituted cycloalkyl of from 3 to 8 carbon atoms, having from 1 to 5 substituents selected from the group consisting of:
- (1) oxo (=O);
  - (2) thioxo (=S);
  - (3) alkoxy as defined in V herein;
  - (4) substituted alkoxy as defined in B<sup>1</sup> herein;
  - (5) acyl as defined in R<sup>1</sup> herein;
  - (6) acylamino as defined in S<sup>1</sup> herein;
  - (7) thiocarbonylamino as defined in B<sup>2</sup> herein;
  - (8) acyloxy as defined in T<sup>1</sup> herein;
  - (9) amino as defined in C7 herein;
  - (10) amidino as defined in C8 herein;

- (11) alkylamidino wherein alkyl is defined in B herein and amidino is defined in C8 herein;
- (12) thioamidino as defined in A<sup>2</sup> herein;
- (13) aminoacyl as defined in U<sup>1</sup> herein;
- (14) aminocarbonylamino as defined in V<sup>1</sup> herein;
- (15) aminothiocabonylamino as defined in W<sup>1</sup> herein;
- (16) aminocarbonyloxy as defined in X<sup>1</sup> herein;
- (17) aryl as defined in J herein;
- (18) substituted aryl as defined in K herein;
- (19) aryloxy as defined in I<sup>1</sup> herein;
- (20) substituted aryloxy as defined in J<sup>1</sup> herein;
- (21) aryloxyaryl as defined in C19 herein;
- (22) substituted aryloxyaryl as defined in C20 herein;
- (23) halogen as defined in Q herein;
- (24) hydroxyl;
- (25) cyano;
- (26) nitro;
- (27) carboxyl;
- (28) carboxylalkyl wherein alkyl is defined in B herein;
- (29) carboxyl-substituted alkyl wherein substituted alkyl is defined in C herein;
- (30) carboxyl-cycloalkyl wherein cycloalkyl is defined in F herein;
- (31) carboxyl-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
- (32) carboxylaryl wherein aryl is defined in J herein;
- (33) carboxyl-substituted aryl wherein substituted aryl is defined in K herein;
- (34) carboxylheteroaryl wherein heteroaryl is defined in L herein;



- (35) carboxyl-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (36) carboxylheterocyclic wherein heterocyclic is defined in N herein;
- (37) carboxyl-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (38) cycloalkyl as defined in F herein;
- (39) substituted cycloalkyl as defined in G herein;
- (40) guanidino as defined in C38 herein;
- (41) guanidinosulfone as defined in C39 herein;
- (42) thiol as defined in X<sup>2</sup> herein;
- (43) thioalkyl as defined in X herein;
- (44) substituted thioalkyl as defined in C42 herein;
- (45) thioaryl as defined in C43 herein;
- (46) substituted thioaryl as defined in C44 herein;
- (47) thiocycloalkyl as defined in C45 herein;
- (48) substituted thiocycloalkyl as defined in C46 herein;
- (49) thioheteroaryl as defined in C47 herein;
- (50) substituted thioheteroaryl as defined in C48 herein;
- (51) thioheterocyclic as defined in C49 herein;
- (52) substituted thioheterocyclic as defined in C50 herein;
- (53) heteroaryl as defined in L herein;
- (54) substituted heteroaryl as defined in M herein;
- (55) heterocyclic as defined in N herein;
- (56) substituted heterocyclic as defined in O herein;
- (57) cycloalkoxy as defined in E<sup>1</sup> herein;
- (58) substituted cycloalkoxy as defined in F<sup>1</sup> herein;
- (59) heteroaryloxy as defined in K<sup>1</sup> herein;
- (60) substituted heteroaryloxy as defined in L<sup>1</sup> herein;

- (61) heterocyclyloxy as defined in M<sup>1</sup> herein;
- (62) substituted heterocyclyloxy as defined in N<sup>1</sup> herein;
- (63) oxycarbonylamino as defined in Y<sup>1</sup> herein;
- (64) oxythiocarbonylamino as defined in Z<sup>1</sup> herein;
- (65) -OS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (66) -OS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (67) -OS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (68) -OS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (69) -OS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (70) -OS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (71) -OS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (72) -OS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (73) -OSO<sub>2</sub>-NRR where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;
- (74) -NRS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (75) -NRS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (76) -NRS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (77) -NRS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (78) -NRS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (79) -NRS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;

- (80) -NRS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (81) -NRS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (82) -NRS(O)<sub>2</sub>-NR-alkyl wherein alkyl is defined in B herein;
- (83) -NRS(O)<sub>2</sub>-NR-substituted alkyl wherein substituted alkyl is defined in C herein;
- (84) -NRS(O)<sub>2</sub>-NR-aryl wherein aryl is defined in J herein;
- (85) -NRS(O)<sub>2</sub>-NR-substituted aryl wherein substituted aryl is defined in K herein;
- (86) -NRS(O)<sub>2</sub>-NR-heteroaryl wherein heteroaryl is defined in L herein;
- (87) -NRS(O)<sub>2</sub>-NR-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (88) -NRS(O)<sub>2</sub>-NR-heterocyclic wherein heterocyclic is defined in N herein;
- (89) -NRS(O)<sub>2</sub>-NR-substituted heterocyclic wherein substituted heterocyclic is defined in O herein and where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;
- (90) mono- and di-alkylamino wherein alkylamino is defined in I<sup>29</sup> herein;
- (91) mono- and di-(substituted alkyl)amino wherein substituted alkylamino is defined in I<sup>210</sup> herein;
- (92) mono- and di-arylamino wherein aryl is defined in J herein and amino is defined in C7 herein;
- (93) mono- and di-substituted arylamino wherein substituted aryl is defined in K herein and amino is defined in C7 herein;

- (94) mono- and di-heteroaryl amino wherein heteroaryl is defined in L herein and amino is defined in C7 herein;
- (95) mono- and di-substituted heteroaryl amino wherein substituted heteroaryl is defined in M herein and amino is defined in C7 herein;
- (96) mono- and di-heterocyclic amino wherein heterocyclic is defined in N herein and amino is defined in C7 herein;
- (97) mono- and di-substituted heterocyclic amino wherein substituted heterocyclic is defined in O herein and amino is defined in C7 herein;
- (98) unsymmetric di-substituted amines having different substituents selected from:
  - (a) alkyl as defined in B herein;
  - (b) substituted alkyl as defined in C herein;
  - (c) aryl as defined in J herein;
  - (d) substituted aryl as defined in K herein;
  - (e) heteroaryl as defined in L herein;
  - (f) substituted heteroaryl as defined in M herein;
  - (g) heterocyclic as defined in N herein;
  - (h) substituted heterocyclic as defined in O herein; and
  - (i) substituted alkynyl groups having amino groups blocked by conventional blocking groups such as Boc, Cbz, formyl, and the like or alkynyl/substituted alkynyl groups substituted with:
    - (i) -SO<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
    - (ii) -SO<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;

- (iii) -SO<sub>2</sub>-alkenyl wherein alkenyl is defined in D herein;
  - (iv) -SO<sub>2</sub>-substituted alkenyl wherein substituted alkenyl is defined in E herein;
  - (v) -SO<sub>2</sub>-cycloalkyl wherein cycloalkyl is defined in F herein;
  - (vi) -SO<sub>2</sub>-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
  - (vii) -SO<sub>2</sub>-aryl wherein aryl is defined in J herein;
  - (viii) -SO<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
  - (ix) -SO<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
  - (x) -SO<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
  - (xi) -SO<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
  - (xii) -SO<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein; and
  - (xiii) -SO<sub>2</sub>NRR where R is:
    - (a) hydrogen; or
    - (b) alkyl as defined in B herein;
- H) cycloalkenyl of from 3 to 8 carbon atoms;
- I) substituted cycloalkenyl of from 3 to 8 carbon atoms, having from 1 to 5 substituents selected from the group consisting of:

- (1) oxo (=O);
- (2) thioxo (=S);
- (3) alkoxy as defined in V herein;
- (4) substituted alkoxy as defined in B<sup>1</sup> herein;
- (5) acyl as defined in R<sup>1</sup> herein;
- (6) acylamino as defined in S<sup>1</sup> herein;
- (7) thiocarbonylamino as defined in B<sup>2</sup> herein;
- (8) acyloxy as defined in T<sup>1</sup> herein;
- (9) amino as defined in C7 herein;
- (10) amidino as defined in C8 herein;
- (11) alkylamidino wherein alkyl is defined in B herein and amidino is defined in C8 herein;
- (12) thioamidino as defined in A<sup>2</sup> herein;
- (13) aminoacyl as defined in U<sup>1</sup> herein;
- (14) aminocarbonylamino as defined in V<sup>1</sup> herein;
- (15) aminothiocabonylamino as defined in W<sup>1</sup> herein;
- (16) aminocarbonyloxy as defined in X<sup>1</sup> herein;
- (17) aryl as defined in J herein;
- (18) substituted aryl as defined in K herein;
- (19) aryloxy as defined in I<sup>1</sup> herein;
- (20) substituted aryloxy as defined in J<sup>1</sup> herein;
- (21) aryloxyaryl as defined in C19 herein;
- (22) substituted aryloxyaryl as defined in C20 herein;
- (23) halogen as defined in Q herein;
- (24) hydroxyl;
- (25) cyano;
- (26) nitro;
- (27) carboxyl;

- (28) carboxylalkyl wherein alkyl is defined in B herein;
- (29) carboxyl-substituted alkyl wherein substituted alkyl is defined in C herein;
- (30) carboxyl-cycloalkyl wherein cycloalkyl is defined in F herein;
- (31) carboxyl-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
- (32) carboxylaryl wherein aryl is defined in J herein;
- (33) carboxyl-substituted aryl wherein substituted aryl is defined in K herein;
- (34) carboxylheteroaryl wherein heteroaryl is defined in L herein;
- (35) carboxyl-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (36) carboxylheterocyclic wherein heterocyclic is defined in N herein;
- (37) carboxyl-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (38) cycloalkyl as defined in F herein;
- (39) substituted cycloalkyl as defined in G herein;
- (40) guanidino as defined in C38 herein;
- (41) guanidinosulfone as defined in C39 herein;
- (42) thiol as defined in X<sup>2</sup> herein;
- (43) thioalkyl as defined in X herein;
- (44) substituted thioalkyl as defined in C42 herein;
- (45) thioaryl as defined in C43 herein;
- (46) substituted thioaryl as defined in C44 herein;
- (47) thiocycloalkyl as defined in C45 herein;
- (48) substituted thiocycloalkyl as defined in C46 herein;
- (49) thioheteroaryl as defined in C47 herein;
- (50) substituted thioheteroaryl as defined in C48 herein;

- (51) thioheterocyclic as defined in C49 herein;
- (52) substituted thioheterocyclic as defined in C50 herein;
- (53) heteroaryl as defined in L herein;
- (54) substituted heteroaryl as defined in M herein;
- (55) heterocyclic as defined in N herein;
- (56) substituted heterocyclic as defined in O herein;
- (57) cycloalkoxy as defined in E<sup>1</sup> herein;
- (58) substituted cycloalkoxy as defined in F<sup>1</sup> herein;
- (59) heteroaryloxy as defined in K<sup>1</sup> herein;
- (60) substituted heteroaryloxy as defined in L<sup>1</sup> herein;
- (61) heterocyclyloxy as defined in M<sup>1</sup> herein;
- (62) substituted heterocyclyloxy as defined in N<sup>1</sup> herein;
- (63) oxycarbonylamino as defined in Y<sup>1</sup> herein;
- (64) oxythiocarbonylamino as defined in Z<sup>1</sup> herein;
- (65) -OS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (66) -OS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (67) -OS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (68) -OS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (69) -OS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (70) -OS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (71) -OS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (72) -OS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (73) -OSO<sub>2</sub>-NRR where R is:
  - (a) hydrogen; or



- (b) alkyl as defined in B herein;
- (74) -NRS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (75) -NRS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (76) -NRS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (77) -NRS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (78) -NRS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (79) -NRS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (80) -NRS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (81) -NRS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (82) -NRS(O)<sub>2</sub>-NR-alkyl wherein alkyl is defined in B herein;
- (83) -NRS(O)<sub>2</sub>-NR-substituted alkyl wherein substituted alkyl is defined in C herein;
- (84) -NRS(O)<sub>2</sub>-NR-aryl wherein aryl is defined in J herein;
- (85) -NRS(O)<sub>2</sub>-NR-substituted aryl wherein substituted aryl is defined in K herein;
- (86) -NRS(O)<sub>2</sub>-NR-heteroaryl wherein heteroaryl is defined in L herein;
- (87) -NRS(O)<sub>2</sub>-NR-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (88) -NRS(O)<sub>2</sub>-NR-heterocyclic wherein heterocyclic is defined in N herein;
- (89) -NRS(O)<sub>2</sub>-NR-substituted heterocyclic wherein substituted heterocyclic is defined in O herein and where R is:

- (a) hydrogen; or
  - (b) alkyl as defined in B herein;
- (90) mono- and di-alkylamino wherein alkylamino is defined in I<sup>2</sup>9 herein;
- (91) mono- and di-(substituted alkyl)amino wherein substituted alkylamino is defined in I<sup>2</sup>10 herein;
- (92) mono- and di-arylamino wherein aryl is defined in J herein and amino is defined in C7 herein;
- (93) mono- and di-substituted arylamino wherein substituted aryl is defined in K herein and amino is defined in C7 herein;
- (94) mono- and di-heteroarylamino wherein heteroaryl is defined in L herein and amino is defined in C7 herein;
- (95) mono- and di-substituted heteroarylamino wherein substituted heteroaryl is defined in M herein and amino is defined in C7 herein;
- (96) mono- and di-heterocyclic amino wherein heterocyclic is defined in N herein and amino is defined in C7 herein;
- (97) mono- and di-substituted heterocyclic amino wherein substituted heterocyclic is defined in O herein and amino is defined in C7 herein;
- (98) unsymmetric di-substituted amines having different substituents selected from:
- (a) alkyl as defined in B herein;
  - (b) substituted alkyl as defined in C herein;
  - (c) aryl as defined in J herein;
  - (d) substituted aryl as defined in K herein;
  - (e) heteroaryl as defined in L herein;
  - (f) substituted heteroaryl as defined in M herein;

- (g) heterocyclic as defined in N herein;
- (h) substituted heterocyclic as defined in O herein; and
- (i) substituted alkynyl groups having amino groups blocked by conventional blocking groups such as Boc, Cbz, formyl, and the like or alkynyl/substituted alkynyl groups substituted with:
  - (i) -SO<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
  - (ii) -SO<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
  - (iii) -SO<sub>2</sub>-alkenyl wherein alkenyl is defined in D herein;
  - (iv) -SO<sub>2</sub>-substituted alkenyl wherein substituted alkenyl is defined in E herein;
  - (v) -SO<sub>2</sub>-cycloalkyl wherein cycloalkyl is defined in F herein;
  - (vi) -SO<sub>2</sub>-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
  - (vii) -SO<sub>2</sub>-aryl wherein aryl is defined in J herein;
  - (viii) -SO<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
  - (ix) -SO<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
  - (x) -SO<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
  - (xi) -SO<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;

- (xii) -SO<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein; and
- (xiii) -SO<sub>2</sub>NRR where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;
- (J) aryl is an unsaturated aromatic carbocyclic group of from 6 to 14 carbon atoms;
- (K) substituted aryl of from 1 to 3 substituents selected from the group consisting of:
  - (1) hydroxy;
  - (2) acyl as defined in R<sup>1</sup> herein;
  - (3) acylamino as defined in S<sup>1</sup> herein;
  - (4) thiocarbonylamino as defined in B<sup>2</sup> herein;
  - (5) acyloxy as defined in T<sup>1</sup> herein;
  - (6) alkyl as defined in B herein;
  - (7) substituted alkyl as defined in C herein;
  - (8) alkoxy as defined in V herein;
  - (9) substituted alkoxy as defined in B<sup>1</sup> herein;
  - (10) alkenyl as defined in D herein;
  - (11) substituted alkenyl as defined in E herein;
  - (12) alkynyl as defined in U herein;
  - (13) substituted alkynyl as defined in Q<sup>231</sup> herein;
  - (14) amidino as defined in C8 herein;
  - (15) alkylamidino wherein alkyl is defined in B herein and amidino is defined in C8 herein;
  - (16) thioamidino as defined in A<sup>2</sup> herein;
  - (17) amino as defined in C7 herein;

- (18) aminoacyl as defined in U<sup>1</sup> herein;
- (19) aminocarbonyloxy as defined in X<sup>1</sup> herein;
- (20) aminocarbonylamino as defined in V<sup>1</sup> herein;
- (21) aminothiocabonylamino as defined in W<sup>1</sup> herein;
- (22) aryl as defined in J herein;
- (23) substituted aryl as defined in K herein;
- (24) aryloxy as defined in I<sup>1</sup> herein;
- (25) substituted aryloxy as defined in J<sup>1</sup> herein;
- (26) cycloalkoxy as defined in E<sup>1</sup> herein;
- (27) substituted cycloalkoxy as defined in F<sup>1</sup> herein;
- (28) heteroaryloxy as defined in K<sup>1</sup> herein;
- (29) substituted heteroaryloxy as defined in L<sup>1</sup> herein;
- (30) heterocyclyloxy as defined in M<sup>1</sup> herein;
- (31) substituted heterocyclyloxy as defined in N<sup>1</sup> herein;
- (32) carboxyl;
- (33) carboxylalkyl wherein alkyl is defined in B herein;
- (34) carboxyl-substituted alkyl wherein substituted alkyl is defined in C herein;
- (35) carboxyl-cycloalkyl wherein cycloalkyl is defined in F herein;
- (36) carboxyl-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
- (37) carboxylaryl wherein aryl is defined in J herein;
- (38) carboxyl-substituted aryl wherein substituted aryl is defined in K herein;
- (39) carboxylheteroaryl wherein heteroaryl is defined in L herein;
- (40) carboxyl-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (41) carboxylheterocyclic wherein heterocyclic is defined in N herein;

- (42) carboxyl-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (43) carboxylamido;
- (44) cyano;
- (45) thiol as defined in X<sup>2</sup> herein;
- (46) thioalkyl as defined in X herein;
- (47) substituted thioalkyl as defined in C42 herein;
- (48) thioaryl as defined in C43 herein;
- (49) substituted thioaryl as defined in C44 herein;
- (50) thioheteroaryl as defined in C47 herein;
- (51) substituted thioheteroaryl as defined in C48 herein;
- (52) thiocycloalkyl as defined in C45 herein;
- (53) substituted thiocycloalkyl as defined in C46 herein;
- (54) thioheterocyclic as defined in C49 herein;
- (55) substituted thioheterocyclic as defined in C50 herein;
- (56) cycloalkyl as defined in F herein;
- (57) substituted cycloalkyl as defined in G herein;
- (58) guanidino as defined in C38 herein;
- (59) guanidinosulfone as defined in C39 herein;
- (60) halo as defined in Q herein;
- (61) nitro;
- (62) heteroaryl as defined in L herein;
- (63) substituted heteroaryl as defined in M herein;
- (64) heterocyclic as defined in N herein;
- (65) substituted heterocyclic as defined in O herein;
- (66) cycloalkoxy as defined in E<sup>1</sup> herein;
- (67) substituted cycloalkoxy as defined in F<sup>1</sup> herein;
- (68) heteroaryloxy as defined in K<sup>1</sup> herein;

- (69) substituted heteroaryloxy as defined in L<sup>1</sup> herein;
- (70) heterocyclyloxy as defined in M<sup>1</sup> herein;
- (71) substituted heterocyclyloxy as defined in N<sup>1</sup> herein;
- (72) oxycarbonylamino as defined in Y<sup>1</sup> herein;
- (73) oxythiocarbonylamino as defined in Z<sup>1</sup> herein;
- (74) -S(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (75) -S(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (76) -S(O)<sub>2</sub>-cycloalkyl wherein cycloalkyl is defined in F herein;
- (77) -S(O)<sub>2</sub>-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
- (78) -S(O)<sub>2</sub>-alkenyl wherein alkenyl is defined in D herein;
- (79) -S(O)<sub>2</sub>-substituted alkenyl wherein substituted alkenyl is defined in E herein;
- (80) -S(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (81) -S(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (82) -S(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (83) -S(O)<sub>2</sub>-substituted heteroaryl wherein substituted aryl is defined in M herein;
- (84) -S(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (85) -S(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (86) -OS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (87) -OS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (88) -OS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;

- (89) -OS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (90) -OS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (91) -OS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (92) -OS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (93) -OS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (94) -OSO<sub>2</sub>-NRR where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;
- (95) -NRS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (96) -NRS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (97) -NRS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (98) -NRS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (99) -NRS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (100) -NRS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (101) -NRS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (102) -NRS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (103) -NRS(O)<sub>2</sub>-NR-alkyl wherein alkyl is defined in B herein;
- (104) -NRS(O)<sub>2</sub>-NR-substituted alkyl wherein substituted alkyl is defined in C herein;
- (105) -NRS(O)<sub>2</sub>-NR-aryl wherein aryl is defined in J herein;



- (106) -NRS(O)<sub>2</sub>-NR-substituted aryl wherein substituted aryl is defined in K herein;
- (107) -NRS(O)<sub>2</sub>-NR-heteroaryl wherein heteroaryl is defined in L herein;
- (108) -NRS(O)<sub>2</sub>-NR-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (109) -NRS(O)<sub>2</sub>-NR-heterocyclic wherein heterocyclic is defined in N herein;
- (110) -NRS(O)<sub>2</sub>-NR-substituted heterocyclic wherein substituted heterocyclic is defined in O herein and where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;
- (111) mono- and di-alkylamino wherein alkylamino is defined in I<sup>29</sup> herein;
- (112) mono- and di-(substituted alkyl)amino wherein substituted alkylamino is defined in I<sup>210</sup> herein;
- (113) mono- and di-arylamino wherein aryl is defined in J herein and amino is defined in C7 herein;
- (114) mono- and di-substituted arylamino wherein substituted aryl is defined in K herein and amino is defined in C7 herein;
- (115) mono- and di-heteroarylamino wherein heteroaryl is defined in L herein and amino is defined in C7 herein;
- (116) mono- and di-substituted heteroarylamino wherein substituted heteroaryl is defined in M herein and amino is defined in C7 herein;

- (117) mono- and di-heterocyclic amino wherein heterocyclic is defined in N herein and amino is defined in C7 herein;
- (118) mono- and di-substituted heterocyclic amino wherein substituted heterocyclic is defined in O herein and amino is defined in C7 herein;
- (119) unsymmetric di-substituted amines having different substituents selected from:
  - (a) alkyl as defined in B herein;
  - (b) substituted alkyl as defined in C herein;
  - (c) aryl as defined in J herein;
  - (d) substituted aryl as defined in K herein;
  - (e) heteroaryl as defined in L herein;
  - (f) substituted heteroaryl as defined in M herein;
  - (g) heterocyclic as defined in N herein;
  - (h) substituted heterocyclic as defined in O herein; and
  - (i) amino groups, as defined in C7 herein, on the substituted aryl blocked by conventional blocking groups such as Boc, Cbz, formyl, and the like or substituted with -SO<sub>2</sub>NRR where R is:
    - (i) hydrogen; or
    - (ii) alkyl as defined in B herein;
- (L) heteroaryl of from 2 to 10 carbon atoms and 1 to 4 heteroatoms selected from oxygen, nitrogen and sulfur within the ring or oxides thereof;
- (M) substituted heteroaryl of from 2 to 10 carbon atoms and 1 to 4 heteroatoms selected from oxygen, nitrogen and sulfur within the ring or oxides thereof, which are substituted with from 1 to 3 substituents selected from the group consisting of:

- (1) hydroxy;
- (2) acyl as defined in R<sup>1</sup> herein;
- (3) acylamino as defined in S<sup>1</sup> herein;
- (4) thiocarbonylamino as defined in B<sup>2</sup> herein;
- (5) acyloxy as defined in T<sup>1</sup> herein;
- (6) alkyl as defined in B herein;
- (7) substituted alkyl as defined in C herein;
- (8) alkoxy as defined in V herein;
- (9) substituted alkoxy as defined in B<sup>1</sup> herein;
- (10) alkenyl as defined in D herein;
- (11) substituted alkenyl as defined in E herein;
- (12) alkynyl as defined in U herein;
- (13) substituted alkynyl as defined in Q<sup>231</sup> herein;
- (14) amidino as defined in C8 herein;
- (15) alkylamidino wherein alkyl is defined in B herein and amidino is defined in C8 herein;
- (16) thioamidino as defined in A<sup>2</sup> herein;
- (17) amino as defined in C7 herein;
- (18) aminoacyl as defined in U<sup>1</sup> herein;
- (19) aminocarbonyloxy as defined in X<sup>1</sup> herein;
- (20) aminocarbonylamino as defined in V<sup>1</sup> herein;
- (21) aminothiocabonylamino as defined in W<sup>1</sup> herein;
- (22) aryl as defined in J herein;
- (23) substituted aryl as defined in K herein;
- (24) aryloxy as defined in I<sup>1</sup> herein;
- (25) substituted aryloxy as defined in J<sup>1</sup> herein;
- (26) cycloalkoxy as defined in E<sup>1</sup> herein;
- (27) substituted cycloalkoxy as defined in F<sup>1</sup> herein;

- (28) heteroaryloxy as defined in K<sup>1</sup> herein;
- (29) substituted heteroaryloxy as defined in L<sup>1</sup> herein;
- (30) heterocyclyloxy as defined in M<sup>1</sup> herein;
- (31) substituted heterocyclyloxy as defined in N<sup>1</sup> herein;
- (32) carboxyl;
- (33) carboxylalkyl wherein alkyl is defined in B herein;
- (34) carboxyl-substituted alkyl wherein substituted alkyl is defined in C herein;
- (35) carboxyl-cycloalkyl wherein cycloalkyl is defined in F herein;
- (36) carboxyl-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
- (37) carboxylaryl wherein aryl is defined in J herein;
- (38) carboxyl-substituted aryl wherein substituted aryl is defined in K herein;
- (39) carboxylheteroaryl wherein heteroaryl is defined in L herein;
- (40) carboxyl-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (41) carboxylheterocyclic wherein heterocyclic is defined in N herein;
- (42) carboxyl-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (43) carboxylamido;
- (44) cyano;
- (45) thiol as defined in X<sup>2</sup> herein;
- (46) thioalkyl as defined in X herein;
- (47) substituted thioalkyl as defined in C42 herein;
- (48) thioaryl as defined in C43 herein;
- (49) substituted thioaryl as defined in C44 herein;
- (50) thioheteroaryl as defined in C47 herein;

- (51) substituted thioheteroaryl as defined in C48 herein;
- (52) thiocycloalkyl as defined in C45 herein;
- (53) substituted thiocycloalkyl as defined in C46 herein;
- (54) thioheterocyclic as defined in C49 herein;
- (55) substituted thioheterocyclic as defined in C50 herein;
- (56) cycloalkyl as defined in F herein;
- (57) substituted cycloalkyl as defined in G herein;
- (58) guanidino as defined in C38 herein;
- (59) guanidinosulfone as defined in C39 herein;
- (60) halo as defined in Q herein;
- (61) nitro;
- (62) heteroaryl as defined in L herein;
- (63) substituted heteroaryl as defined in M herein;
- (64) heterocyclic as defined in N herein;
- (65) substituted heterocyclic as defined in O herein;
- (66) cycloalkoxy as defined in E<sup>1</sup> herein;
- (67) substituted cycloalkoxy as defined in F<sup>1</sup> herein;
- (68) heteroaryloxy as defined in K<sup>1</sup> herein;
- (69) substituted heteroaryloxy as defined in L<sup>1</sup> herein;
- (70) heterocyclyloxy as defined in M<sup>1</sup> herein;
- (71) substituted heterocyclyloxy as defined in N<sup>1</sup> herein;
- (72) oxycarbonylamino as defined in Y<sup>1</sup> herein;
- (73) oxythiocarbonylamino as defined in Z<sup>1</sup> herein;
- (74) -S(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (75) -S(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (76) -S(O)<sub>2</sub>-cycloalkyl wherein cycloalkyl is defined in F herein;

- (77) -S(O)<sub>2</sub>-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
- (78) -S(O)<sub>2</sub>-alkenyl wherein alkenyl is defined in D herein;
- (79) -S(O)<sub>2</sub>-substituted alkenyl wherein substituted alkenyl is defined in E herein;
- (80) -S(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (81) -S(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (82) -S(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (83) -S(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (84) -S(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (85) -S(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (86) -OS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (87) -OS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (88) -OS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (89) -OS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (90) -OS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (91) -OS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (92) -OS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (93) -OS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (94) -OSO<sub>2</sub>-NRR where R is:
  - (a) hydrogen; or

- (b) alkyl as defined in B herein;
- (95) -NRS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (96) -NRS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (97) -NRS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (98) -NRS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (99) -NRS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (100) -NRS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (101) -NRS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (102) -NRS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (103) -NRS(O)<sub>2</sub>-NR-alkyl wherein alkyl is defined in B herein;
- (104) -NRS(O)<sub>2</sub>-NR-substituted alkyl wherein substituted alkyl is defined in C herein;
- (105) -NRS(O)<sub>2</sub>-NR-aryl wherein aryl is defined in J herein;
- (106) -NRS(O)<sub>2</sub>-NR-substituted aryl wherein substituted aryl is defined in K herein;
- (107) -NRS(O)<sub>2</sub>-NR-heteroaryl wherein heteroaryl is defined in L herein;
- (108) -NRS(O)<sub>2</sub>-NR-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (109) -NRS(O)<sub>2</sub>-NR-heterocyclic wherein heterocyclic is defined in N herein;

- (110) -NRS(O)<sub>2</sub>-NR-substituted heterocyclic wherein substituted heterocyclic is defined in O herein and where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;
- (111) mono- and di-alkylamino wherein alkylamino is defined in I<sup>29</sup> herein;
- (112) mono- and di-(substituted alkyl)amino wherein substituted alkylamino is defined in I<sup>210</sup> herein;
- (113) mono- and di-arylamino wherein aryl is defined in J herein and amino is defined in C7 herein;
- (114) mono- and di-substituted arylamino wherein substituted aryl is defined in K herein and amino is defined in C7 herein;
- (115) mono- and di-heteroarylamino wherein heteroaryl is defined in L herein and amino is defined in C7 herein;
- (116) mono- and di-substituted heteroarylamino wherein substituted heteroaryl is defined in M herein and amino is defined in C7 herein;
- (117) mono- and di-heterocyclic amino wherein heterocyclic is defined in N herein and amino is defined in C7 herein;
- (118) mono- and di-substituted heterocyclic amino wherein substituted heterocyclic is defined in O herein and amino is defined in C7 herein;
- (119) unsymmetric di-substituted amines having different substituents selected from:
  - (a) alkyl as defined in B herein;
  - (b) substituted alkyl as defined in C herein;



- (c) aryl as defined in J herein;
  - (d) substituted aryl as defined in K herein;
  - (e) heteroaryl as defined in L herein;
  - (f) substituted heteroaryl as defined in M herein;
  - (g) heterocyclic as defined in N herein;
  - (h) substituted heterocyclic as defined in O herein; and
  - (i) amino groups, as defined in C7 herein, on the substituted aryl blocked by conventional blocking groups such as Boc, Cbz, formyl, and the like or substituted with -SO<sub>2</sub>NRR where R is:
    - (i) hydrogen; or
    - (ii) alkyl as defined in B herein;
- (N) heterocyclic of from 1 to 10 carbon atoms and from 1 to 4 heteroatoms selected from nitrogen, sulfur or oxygen within the ring, wherein one or more of the rings can be aryl, as defined in J herein, or heteroaryl as defined in L herein; and
- (O) substituted heterocyclic of from 1 to 10 carbon atoms and from 1 to 4 heteroatoms which are substituted with from 1 to 3 substituents selected from the group consisting of:
- (1) oxo (=O);
  - (2) thioxo (=S);
  - (3) alkoxy as defined in V herein;
  - (4) substituted alkoxy as defined in B<sup>1</sup> herein;
  - (5) acyl as defined in R<sup>1</sup> herein;
  - (6) acylamino as defined in S<sup>1</sup> herein;
  - (7) thiocarbonylamino as defined in B<sup>2</sup> herein;
  - (8) acyloxy as defined in T<sup>1</sup> herein;
  - (9) amino as defined in C7 herein;

- (10) amidino as defined in C8 herein;
- (11) alkylamidino wherein alkyl is defined in B herein and amidino is defined in C8 herein;
- (12) thioamidino as defined in A<sup>2</sup> herein;
- (13) aminoacyl as defined in U<sup>1</sup> herein;
- (14) aminocarbonylamino as defined in V<sup>1</sup> herein;
- (15) aminothiocarbonylamino as defined in W<sup>1</sup> herein;
- (16) aminocarbonyloxy as defined in X<sup>1</sup> herein;
- (17) aryl as defined in J herein;
- (18) substituted aryl as defined in K herein;
- (19) aryloxy as defined in I<sup>1</sup> herein;
- (20) substituted aryloxy as defined in J<sup>1</sup> herein;
- (21) aryloxyaryl as defined in C19 herein;
- (22) substituted aryloxyaryl as defined in C20 herein;
- (23) halogen as defined in Q herein;
- (24) hydroxyl;
- (25) cyano;
- (26) nitro;
- (27) carboxyl;
- (28) carboxylalkyl wherein alkyl is defined in B herein;
- (29) carboxyl-substituted alkyl wherein substituted alkyl is defined in C herein;
- (30) carboxyl-cycloalkyl wherein cycloalkyl is defined in F herein;
- (31) carboxyl-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
- (32) carboxylaryl wherein aryl is defined in J herein;
- (33) carboxyl-substituted aryl wherein substituted aryl is defined in K herein;

- (34) carboxylheteroaryl wherein heteroaryl is defined in L herein;
- (35) carboxyl-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (36) carboxylheterocyclic wherein heterocyclic is defined in N herein;
- (37) carboxyl-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (38) cycloalkyl as defined in F herein;
- (39) substituted cycloalkyl as defined in G herein;
- (40) guanidino as defined in C38 herein;
- (41) guanidinosulfone as defined in C39 herein;
- (42) thiol as defined in X<sup>2</sup> herein;
- (43) thioalkyl as defined in X herein;
- (44) substituted thioalkyl as defined in C42 herein;
- (45) thioaryl as defined in C43 herein;
- (46) substituted thioaryl as defined in C44 herein;
- (47) thiocycloalkyl as defined in C45 herein;
- (48) substituted thiocycloalkyl as defined in C46 herein;
- (49) thioheteroaryl as defined in C47 herein;
- (50) substituted thioheteroaryl as defined in C48 herein;
- (51) thioheterocyclic as defined in C49 herein;
- (52) substituted thioheterocyclic as defined in C50 herein;
- (53) heteroaryl as defined in L herein;
- (54) substituted heteroaryl as defined in M herein;
- (55) heterocyclic as defined in N herein;
- (56) substituted heterocyclic as defined in O herein;
- (57) cycloalkoxy as defined in E<sup>1</sup> herein;
- (58) substituted cycloalkoxy as defined in F<sup>1</sup> herein;
- (59) heteroaryloxy as defined in K<sup>1</sup> herein;

- (60) substituted heteroaryloxy as defined in L<sup>1</sup> herein;
- (61) heterocyclyloxy as defined in M<sup>1</sup> herein;
- (62) substituted heterocyclyloxy as defined in N<sup>1</sup> herein;
- (63) oxycarbonylamino as defined in Y<sup>1</sup> herein;
- (64) oxythiocarbonylamino as defined in Z<sup>1</sup> herein;
- (65) -OS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (66) -OS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (67) -OS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (68) -OS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (69) -OS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (70) -OS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (71) -OS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (72) -OS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (73) -OSO<sub>2</sub>-NRR where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;
- (74) -NRS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (75) -NRS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (76) -NRS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (77) -NRS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (78) -NRS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;

- (79) -NRS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (80) -NRS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (81) -NRS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (82) -NRS(O)<sub>2</sub>-NR-alkyl wherein alkyl is defined in B herein;
- (83) -NRS(O)<sub>2</sub>-NR-substituted alkyl wherein substituted alkyl is defined in C herein;
- (84) -NRS(O)<sub>2</sub>-NR-aryl wherein aryl is defined in J herein;
- (85) -NRS(O)<sub>2</sub>-NR-substituted aryl wherein substituted aryl is defined in K herein;
- (86) -NRS(O)<sub>2</sub>-NR-heteroaryl wherein heteroaryl is defined in L herein;
- (87) -NRS(O)<sub>2</sub>-NR-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (88) -NRS(O)<sub>2</sub>-NR-heterocyclic wherein heterocyclic is defined in N herein;
- (89) -NRS(O)<sub>2</sub>-NR-substituted heterocyclic wherein substituted heterocyclic is defined in O herein and where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;
- (90) mono- and di-alkylamino wherein alkylamino is defined in I<sup>29</sup> herein;
- (91) mono- and di-(substituted alkyl)amino wherein substituted alkylamino is defined in I<sup>210</sup> herein;
- (92) mono- and di-arylamino wherein aryl is defined in J herein and amino is defined in C7 herein;

- (93) mono- and di-substituted arylamino wherein substituted aryl is defined in K herein and amino is defined in C7 herein;
- (94) mono- and di-heteroarylamino wherein heteroaryl is defined in L herein and amino is defined in C7 herein;
- (95) mono- and di-substituted heteroarylamino wherein substituted heteroaryl is defined in M herein and amino is defined in C7 herein;
- (96) mono- and di-heterocyclic amino wherein heterocyclic is defined in N herein and amino is defined in C7 herein;
- (97) mono- and di-substituted heterocyclic amino wherein substituted heterocyclic is defined in O herein and amino is defined in C7 herein;
- (98) unsymmetric di-substituted amines having different substituents selected from:
  - (a) alkyl as defined in B herein;
  - (b) substituted alkyl as defined in C herein;
  - (c) aryl as defined in J herein;
  - (d) substituted aryl as defined in K herein;
  - (e) heteroaryl as defined in L herein;
  - (f) substituted heteroaryl as defined in M herein;
  - (g) heterocyclic as defined in N herein;
  - (h) substituted heterocyclic as defined in O herein; and
  - (i) substituted alkynyl groups, wherein substituted alkynyl is defined in Q<sup>2</sup>31 herein, having amino groups blocked by conventional blocking groups such as Boc, Cbz, formyl, and the like or alkynyl/ groups substituted with:
    - (i) -SO<sub>2</sub>-alkyl wherein alkyl is defined in B herein;

- (ii) -SO<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (iii) -SO<sub>2</sub>-alkenyl wherein alkenyl is defined in D herein;
- (iv) -SO<sub>2</sub>-substituted alkenyl wherein substituted alkenyl is defined in E herein;
- (v) -SO<sub>2</sub>-cycloalkyl wherein cycloalkyl is defined in F herein;
- (vi) -SO<sub>2</sub>-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
- (vii) -SO<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (viii) -SO<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (ix) -SO<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (x) -SO<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (xi) -SO<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (xii) -SO<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein; and
- (xiii) -SO<sub>2</sub>NRR where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;

R<sup>3</sup> and R<sup>3a</sup> are independently selected from the group consisting of:

- (P) hydrogen;
- (Q) halogen or halo referring to fluoro, chloro, bromo and iodo;
- (R) alkyl as defined in B above;
- (S) substituted alkyl as defined in C above;
- (T) alkenyl as defined in D herein;
- (U) alkynyl of from 2 to 10 carbon atoms and from 1-2 sites of alkynyl unsaturation;
- (V) alkoxy having the formula "alkyl-O-";
- (W) haloalkoxy wherein halo is defined in Q herein and alkoxy is defined in V herein;
- (X) thioalkyl having the formula "-S-alkyl"; or
- (Y)  $-(\text{Alk}^b)_m\text{R}^b$  in which  $\text{Alk}^b$  is a  $\text{C}_{1-3}$  alkylene chain, m is 0 or 1 and  $\text{R}^b$  is:
  - (1) hydroxy;
  - (2) thiol as defined in X<sup>2</sup> herein;
  - (3) nitro;
  - (4) cyano;
  - (5) carboxy;
  - (6)  $-\text{CO}_2\text{R}^c$  wherein  $\text{R}^c$  is alkyl as defined in B herein;
  - (7)  $-\text{SO}_3\text{H}$ ;
  - (8)  $-\text{SOR}^c$  wherein  $\text{R}^c$  is alkyl as defined in B herein;
  - (9)  $-\text{SO}_2\text{R}^c$  wherein  $\text{R}^c$  is alkyl as defined in B herein;
  - (10)  $-\text{SO}_3\text{R}^c$  wherein  $\text{R}^c$  is alkyl as defined in B herein;
  - (11)  $-\text{OCO}_2\text{R}^c$  wherein  $\text{R}^c$  is alkyl as defined in B herein;
  - (12)  $-\text{C}(\text{O})\text{H}$ ;
  - (13)  $-\text{COR}^c$  wherein  $\text{R}^c$  is alkyl as defined in B herein;
  - (14)  $-\text{OCOR}^c$  wherein  $\text{R}^c$  is alkyl as defined in B herein;
  - (15)  $-\text{CSR}^c$  wherein  $\text{R}^c$  is alkyl as defined in B herein;



- (16)  $-\text{Nr}^{\text{d}}\text{R}^{\text{e}}$  wherein  $\text{R}^{\text{d}}$  and  $\text{R}^{\text{e}}$  are independently hydrogen, alkyl as defined in B herein, or substituted alkyl as defined in C herein;
- (17)  $-\text{CONR}^{\text{d}}\text{R}^{\text{e}}$  wherein  $\text{R}^{\text{d}}$  and  $\text{R}^{\text{e}}$  are independently hydrogen, alkyl as defined in B herein, or substituted alkyl as defined in C herein;
- (18)  $-\text{OCONR}^{\text{d}}\text{R}^{\text{e}}$  wherein  $\text{R}^{\text{d}}$  and  $\text{R}^{\text{e}}$  are independently hydrogen, alkyl as defined in B herein, or substituted alkyl as defined in C herein;
- (19)  $-\text{Nr}^{\text{d}}\text{COR}^{\text{e}}$  wherein  $\text{R}^{\text{d}}$  and  $\text{R}^{\text{e}}$  are independently hydrogen, alkyl as defined in B herein, or substituted alkyl as defined in C herein;
- (20)  $-\text{CSNR}^{\text{d}}\text{R}^{\text{e}}$  wherein  $\text{R}^{\text{d}}$  and  $\text{R}^{\text{e}}$  are independently hydrogen, alkyl as defined in B herein, or substituted alkyl as defined in C herein;
- (21)  $-\text{Nr}^{\text{d}}\text{CSR}^{\text{e}}$  wherein  $\text{R}^{\text{d}}$  and  $\text{R}^{\text{e}}$  are independently hydrogen, alkyl as defined in B herein, or substituted alkyl as defined in C herein;
- (22)  $-\text{SO}_2\text{NR}^{\text{d}}\text{R}^{\text{e}}$  wherein  $\text{R}^{\text{d}}$  and  $\text{R}^{\text{e}}$  are independently hydrogen, alkyl as defined in B herein, or substituted alkyl as defined in C herein;
- (23)  $-\text{Nr}^{\text{d}}\text{SO}_2\text{R}^{\text{e}}$  wherein  $\text{R}^{\text{d}}$  and  $\text{R}^{\text{e}}$  are independently hydrogen, alkyl as defined in B herein, or substituted alkyl as defined in C herein;
- (24)  $-\text{Nr}^{\text{d}}\text{CONR}^{\text{e}}\text{R}^{\text{f}}$  wherein  $\text{R}^{\text{d}}$  and  $\text{R}^{\text{e}}$  are independently hydrogen, alkyl as defined in B herein, or substituted alkyl as defined in C herein; and where  $\text{R}^{\text{f}}$  is hydrogen alkyl as defined in B herein, or substituted alkyl as defined in C herein; or
- (25)  $-\text{Nr}^{\text{d}}\text{SO}_2\text{NR}^{\text{e}}\text{R}^{\text{f}}$  wherein  $\text{R}^{\text{d}}$  and  $\text{R}^{\text{e}}$  are independently hydrogen, alkyl as defined in B herein, or substituted alkyl as defined in C herein; and where  $\text{R}^{\text{f}}$  is hydrogen, alkyl as defined in B herein, or substituted alkyl as defined in C herein.

X is selected from the group consisting of:

- (Z) hydroxyl;

- (A<sup>1</sup>) alkoxy as defined in V herein;
- (B<sup>1</sup>) substituted alkoxy having the formula "substituted alkyl-O-";
- (C<sup>1</sup>) alkenoxy having the formula "alkenyl-O-";
- (D<sup>1</sup>) substituted alkenoxy having the formula "substituted alkenyl-O-";
- (E<sup>1</sup>) cycloalkoxy having the formula "-O-cycloalkyl";
- (F<sup>1</sup>) substituted cycloalkoxy having the formula "-O-substituted cycloalkyl";
- (G<sup>1</sup>) cycloalkenoxyl having the formula "-O-cycloalkenyl";
- (H<sup>1</sup>) substituted cycloalkenoxyl having the formula "-O-substituted cycloalkenyl";
- (I<sup>1</sup>) aryloxy having the formula "aryl-O-";
- (J<sup>1</sup>) substituted aryloxy having the formula "substituted aryl-O-";
- (K<sup>1</sup>) heteroaryloxy having the formula "-O-heteroaryl";
- (L<sup>1</sup>) substituted heteroaryloxy having the formula "-O-substituted heteroaryl";
- (M<sup>1</sup>) heterocyclyloxy having the formula "-O-heterocyclic";
- (N<sup>1</sup>) substituted heterocyclyloxy having the formula "-O-substituted heterocyclic"; and
- (O<sup>1</sup>) -NR<sup>1</sup>R<sup>2</sup> where each R<sup>1</sup> is independently selected from the group consisting of:
  - (1) hydrogen;
  - (2) alkyl as defined in B herein;
  - (3) substituted alkyl as defined in C herein;
  - (4) alkenyl as defined in D herein;
  - (5) substituted alkenyl as defined in E herein;
  - (6) cycloalkyl as defined in F herein;
  - (7) substituted cycloalkyl as defined in G herein;
  - (8) aryl as defined in J herein;

- (9) substituted aryl as defined in K herein;
- (10) heteroaryl as defined in L herein;
- (11) substituted heteroaryl as defined in M herein;
- (12) heterocyclic as defined in N herein; and
- (13) substituted heterocyclic as defined in O herein;

R<sup>2a</sup> is either:

- (i) an -Ar<sup>1</sup>-R<sup>9</sup> group where Ar<sup>1</sup> is:
  - (P<sup>1</sup>) aryl as defined in J herein; or
  - (Q<sup>1</sup>) heteroaryl, as defined in L herein, optionally substituted with one or two substituents selected from the group consisting of:
    - (1) hydroxy;
    - (2) acyl as defined in R<sup>1</sup> herein;
    - (3) acylamino as defined in S<sup>1</sup> herein;
    - (4) aminoacyl as defined in U<sup>1</sup> herein;
    - (5) acyloxy as defined in T<sup>1</sup> herein;
    - (6) alkyl as defined in B herein;
    - (7) substituted alkyl as defined in C herein;
    - (8) alkoxy as defined in V herein;
    - (9) substituted alkoxy as defined in B<sup>1</sup> herein;
    - (10) amino as defined in C7 herein;
    - (11) aminoacyl as defined in U<sup>1</sup> herein;
    - (12) aminocarbonyloxy as defined in X<sup>1</sup> herein;
    - (13) carboxyl;
    - (14) carboxylalkyl wherein alkyl is defined in B herein;
    - (15) carboxylamido;
    - (16) cyano;
    - (17) thiol as defined in X<sup>2</sup> herein;
    - (18) thioalkyl as defined in X herein;

- (19) substituted thioalkyl as defined in C42 herein;
- (20) halo as defined in Q herein;
- (21) nitro;

provided that said acyl, acylamino, acyloxy, substituted alkyl, substituted alkoxy and substituted thioalkyl do not carry an aryl, substituted aryl, heteroaryl or substituted heteroaryl group; and

R<sup>9</sup> is selected from the group consisting of:

- (R<sup>1</sup>) acyl selected from H-C(O)-, alkyl-C(O)-, substituted alkyl-C(O)-, alkenyl-C(O)-, substituted alkenyl-C(O)-, alkynyl-C(O)-, substituted alkynyl-C(O)-, cycloalkyl-C(O)-, substituted cycloalkyl-C(O)-, aryl-C(O)-, substituted aryl-C(O)-, heteroaryl-C(O)-, substituted heteroaryl-C(O), heterocyclic-C(O)-, and substituted heterocyclic-C(O)-, wherein alkyl is defined in B herein; wherein substituted alkyl is defined in C herein; wherein alkenyl is defined in D herein; wherein substituted alkenyl is defined in E herein; wherein alkynyl is defined in U herein; wherein substituted alkynyl is defined in Q<sup>231</sup> herein; wherein cycloalkyl is defined in F herein; wherein substituted cycloalkyl is defined in G herein; wherein aryl is defined in J herein; wherein substituted aryl is defined in K herein; wherein heteroaryl is defined in L herein; wherein substituted heteroaryl is defined in M herein; wherein heterocyclic is defined in N herein; and wherein substituted heterocyclic is defined in O herein;
- (S<sup>1</sup>) acylamino selected from the group -C(O)NRR where each R is independently selected from the group consisting of:
  - (1) hydrogen;
  - (2) alkyl as defined in B herein;
  - (3) substituted alkyl as defined in C herein;
  - (4) alkenyl as defined in D herein;

- (5) substituted alkenyl as defined in E herein;
- (6) alkynyl as defined in U herein;
- (7) substituted alkynyl as defined in Q<sup>2</sup>31 herein;
- (8) aryl as defined in J herein;
- (9) substituted aryl as defined in K herein;
- (10) cycloalkyl as defined in F herein;
- (11) substituted cycloalkyl as defined in G herein;
- (12) heteroaryl as defined in L herein;
- (13) substituted heteroaryl as defined in M herein;
- (14) heterocyclic as defined in N herein;
- (15) substituted heterocyclic as defined in O herein; and

where each R is joined to form together with the nitrogen atom a heterocyclic or substituted heterocyclic ring wherein alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic are as defined herein.

(T<sup>1</sup>) acyloxy selected from the groups alkyl-C(O)O-, substituted alkyl-C(O)O-, alkenyl-C(O)O-, substituted alkenyl-C(O)O-, alkynyl-C(O)O-, substituted alkynyl-C(O)O-, aryl-C(O)O-, substituted aryl-C(O)O-, cycloalkyl-C(O)O-, substituted cycloalkyl-C(O)O-, heteroaryl-C(O)O-, substituted heteroaryl-C(O)O-, heterocyclic-C(O)O-, and substituted heterocyclic-C(O)O-wherein alkyl is defined in B herein; wherein substituted alkyl is defined in C herein; wherein alkenyl is defined in D herein; wherein substituted alkenyl is defined in E herein; wherein alkynyl is defined in U herein; wherein substituted alkynyl is defined in Q<sup>2</sup>31 herein; wherein cycloalkyl is defined in F herein; wherein substituted cycloalkyl is defined in G herein; wherein aryl is defined in J herein; wherein substituted aryl is defined in K herein; wherein

heteroaryl is defined in L herein; wherein substituted heteroaryl is defined in M herein; wherein heterocyclic is defined in N herein; and wherein substituted heterocyclic is defined in O herein;

- (U<sup>1</sup>) aminoacyl having the formula -NRC(O)alkyl, -NRC(O)substituted alkyl, -NRC(O)cycloalkyl, -NRC(O)substituted cycloalkyl, -NRC(O)alkenyl, -NRC(O)substituted alkenyl, -NRC(O)alkynyl, -NRC(O)substituted alkynyl, -NRC(O)aryl, -NRC(O)substituted aryl, -NRC(O)heteroaryl, -NRC(O) substituted heteroaryl, -NRC(O)heterocyclic, and -NRC(O)substituted heterocyclic where R is hydrogen or alkyl and wherein alkyl is defined in B herein; wherein substituted alkyl is defined in C herein; wherein alkenyl is defined in D herein; wherein substituted alkenyl is defined in E herein; wherein alkynyl is defined in U herein; wherein substituted alkynyl is defined in Q<sup>231</sup> herein; wherein cycloalkyl is defined in F herein; wherein substituted cycloalkyl is defined in G herein; wherein aryl is defined in J herein; wherein substituted aryl is defined in K herein; wherein heteroaryl is defined in L herein; wherein substituted heteroaryl is defined in M herein; wherein heterocyclic is defined in N herein; and wherein substituted heterocyclic is defined in O herein;
- (V<sup>1</sup>) aminocarbonylamino formula -NRC(O)NRR, -NRC(O)NR-alkyl, -NRC(O)NR-substituted alkyl, -NRC(O)NR-alkenyl, -NRC(O)NR-substituted alkenyl, -NRC(O)NR-alkynyl, -NRC(O)NR-substituted alkynyl, -NRC(O)NR-aryl, -NRC(O)NR-substituted aryl, -NRC(O)NR-cycloalkyl, -NRC(O)NR-substituted cycloalkyl, -NRC(O)NR-heteroaryl, and -NRC(O)NR-substituted heteroaryl, -NRC(O)NR-heterocyclic, and -NRC(O)NR-substituted heterocyclic where each R is independently hydrogen, alkyl or where each R is joined to form together with the nitrogen atom a heterocyclic or

substituted heterocyclic ring as well as where one of the amino groups is blocked by conventional blocking groups such as Boc, Cbz, formyl, and the like and wherein alkyl is defined in B herein; wherein substituted alkyl is defined in C herein; wherein alkenyl is defined in D herein; wherein substituted alkenyl is defined in E herein; wherein alkynyl is defined in U herein; wherein substituted alkynyl is defined in Q<sup>2</sup>31 herein; wherein cycloalkyl is defined in F herein; wherein substituted cycloalkyl is defined in G herein; wherein aryl is defined in J herein; wherein substituted aryl is defined in K herein; wherein heteroaryl is defined in L herein; wherein substituted heteroaryl is defined in M herein; wherein heterocyclic is defined in N herein; and wherein substituted heterocyclic is defined in O herein;

(W<sup>1</sup>) aminothiocarbonylamino having the formula -NRC(S)NRR, -NRC(S)NR-alkyl, -NRC(S)NR-substituted alkyl, -NRC(S)NR-alkenyl, -NRC(S)NR-substituted alkenyl, -NRC(S)NR-alkynyl, -NRC(S)NR-substituted alkynyl, -NRC(S)NR-aryl, -NRC(S)NR-substituted aryl, -NRC(S)NR-cycloalkyl, -NRC(S)NR-substituted cycloalkyl, -NRC(S)NR-heteroaryl, and -NRC(S)NR-substituted heteroaryl, -NRC(S)NR-heterocyclic, and -NRC(S)NR-substituted heterocyclic where each R is independently hydrogen, alkyl or where each R is joined to form together with the nitrogen atom a heterocyclic or substituted heterocyclic ring as well as where one of the amino groups is blocked by conventional blocking groups such as Boc, Cbz, formyl, and the like and wherein alkyl is defined in B herein; wherein substituted alkyl is defined in C herein; wherein alkenyl is defined in D herein; wherein substituted alkenyl is defined in E herein; wherein alkynyl is defined in U herein; wherein substituted alkynyl is defined in Q<sup>2</sup>31 herein; wherein cycloalkyl is defined in F herein; wherein

substituted cycloalkyl is defined in G herein; wherein aryl is defined in J herein; wherein substituted aryl is defined in K herein; wherein heteroaryl is defined in L herein; wherein substituted heteroaryl is defined in M herein; wherein heterocyclic is defined in N herein; and wherein substituted heterocyclic is defined in O herein;

(X<sup>1</sup>) aminocarbonyloxy having the formula -NRC(O)O-alkyl, -NRC(O)O-substituted alkyl, -NRC(O)O-alkenyl, -NRC(O)O-substituted alkenyl, -NRC(O)O-alkynyl, -NRC(O)O-substituted alkynyl, -NRC(O)O-cycloalkyl, -NRC(O)O-substituted cycloalkyl, -NRC(O)O-aryl, -NRC(O)O-substituted aryl, -NRC(O)O-heteroaryl, -NRC(O)O-substituted heteroaryl, -NRC(O)O-heterocyclic, and -NRC(O)O-substituted heterocyclic where R is hydrogen or alkyl and wherein alkyl is defined in B herein; wherein substituted alkyl is defined in C herein; wherein alkenyl is defined in D herein; wherein substituted alkenyl is defined in E herein; wherein alkynyl is defined in U herein; wherein substituted alkynyl is defined in Q<sup>231</sup> herein; wherein cycloalkyl is defined in F herein; wherein substituted cycloalkyl is defined in G herein; wherein aryl is defined in J herein; wherein substituted aryl is defined in K herein; wherein heteroaryl is defined in L herein; wherein substituted heteroaryl is defined in M herein; wherein heterocyclic is defined in N herein; and wherein substituted heterocyclic is defined in O herein;

(Y<sup>1</sup>) oxycarbonylamino having the formula -OC(O)NH<sub>2</sub>, -OC(O)NRR, -OC(O)NR-alkyl, -OC(O)NR-substituted alkyl, -OC(O)NR-alkenyl, -OC(O)NR-substituted alkenyl, -OC(O)NR-alkynyl, -OC(O)NR-substituted alkynyl, -OC(O)NR-cycloalkyl, -OC(O)NR-substituted cycloalkyl, -OC(O)NR-aryl, -OC(O)NR-substituted aryl, -OC(O)NR-heteroaryl, -OC(O)NR-substituted heteroaryl, -OC(O)NR-heterocyclic,



and -OC(O)NR-substituted heterocyclic where R is hydrogen, alkyl or where each R is joined to form, together with the nitrogen atom a heterocyclic or substituted heterocyclic ring and wherein alkyl is defined in B herein; wherein substituted alkyl is defined in C herein; wherein alkenyl is defined in D herein; wherein substituted alkenyl is defined in E herein; wherein alkynyl is defined in U herein; wherein substituted alkynyl is defined in Q<sup>231</sup> herein; wherein cycloalkyl is defined in F herein; wherein substituted cycloalkyl is defined in G herein; wherein aryl is defined in J herein; wherein substituted aryl is defined in K herein; wherein heteroaryl is defined in L herein; wherein substituted heteroaryl is defined in M herein; wherein heterocyclic is defined in N herein; and wherein substituted heterocyclic is defined in O herein;

(Z<sup>1</sup>) oxythiocarbonylamino having the formula -OC(S)NH<sub>2</sub>, -OC(S)NRR, -OC(S)NR-alkyl, -OC(S)NR-substituted alkyl, -OC(S)NR-alkenyl, -OC(S)NR-substituted alkenyl, -OC(S)NR-alkynyl, -OC(S)NR-substituted alkynyl, -OC(S)NR-cycloalkyl, -OC(S)NR-substituted cycloalkyl, -OC(S)NR-aryl, -OC(S)NR-substituted aryl, -OC(S)NR-heteroaryl, -OC(S)NR-substituted heteroaryl, -OC(S)NR-heterocyclic, and -OC(S)NR-substituted heterocyclic where R is hydrogen, alkyl or where each R is joined to form together with the nitrogen atom a heterocyclic or substituted heterocyclic ring and wherein alkyl is defined in B herein; wherein substituted alkyl is defined in C herein; wherein alkenyl is defined in D herein; wherein substituted alkenyl is defined in E herein; wherein alkynyl is defined in U herein; wherein substituted alkynyl is defined in Q<sup>231</sup> herein; wherein cycloalkyl is defined in F herein; wherein substituted cycloalkyl is defined in G herein; wherein aryl is defined in J herein; wherein substituted aryl is

defined in K herein; wherein heteroaryl is defined in L herein; wherein substituted heteroaryl is defined in M herein; wherein heterocyclic is defined in N herein; and wherein substituted heterocyclic is defined in O herein;

- (A<sup>2</sup>) thioamidino having the formula "RSC(=NH)-";
- (B<sup>2</sup>) thiocarbonylamino selected from the group -C(S)NRR where each R is independently selected from the group consisting of:
- (1) hydrogen;
  - (2) alkyl as defined in B herein;
  - (3) substituted alkyl as defined in C herein;
  - (4) alkenyl as defined in D herein;
  - (5) substituted alkenyl as defined in E herein;
  - (6) alkynyl as defined in U herein;
  - (7) substituted alkynyl as defined in Q<sup>2</sup>31 herein;
  - (8) aryl as defined in J herein;
  - (9) substituted aryl as defined in K herein;
  - (10) cycloalkyl as defined in F herein;
  - (11) substituted cycloalkyl as defined in G herein;
  - (12) heteroaryl as defined in L herein;
  - (13) substituted heteroaryl as defined in M herein;
  - (14) heterocyclic as defined in N herein;
  - (15) substituted heterocyclic as defined in O herein; and

where each R is joined to form, together with the nitrogen atom a heterocyclic or substituted heterocyclic ring wherein alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, and substituted heterocyclic are as defined herein;

- (C<sup>2</sup>) aminosulfonylamino having the formula -NRSO<sub>2</sub>NRR, -NRSO<sub>2</sub>NR-alkyl, -NRSO<sub>2</sub>NR-substituted alkyl, -NRSO<sub>2</sub>NR-alkenyl, -NRSO<sub>2</sub>NR-substituted alkenyl, -NRSO<sub>2</sub>NR-alkynyl, -NRSO<sub>2</sub>NR-substituted alkynyl, -NRSO<sub>2</sub>NR-aryl, -NRSO<sub>2</sub>NR-substituted aryl, -NRSO<sub>2</sub>NR-cycloalkyl, -NRSO<sub>2</sub>NR-substituted cycloalkyl, -NRSO<sub>2</sub>NR-heteroaryl, and -NRSO<sub>2</sub>NR-substituted heteroaryl, -NRSO<sub>2</sub>NR-heterocyclic, and -NRSO<sub>2</sub>NR-substituted heterocyclic, where each R is independently hydrogen, alkyl or where each R is joined to form together with the nitrogen atom a heterocyclic or substituted heterocyclic ring as well as where one of the amino groups is blocked by conventional blocking groups such as Boc, Cbz, formyl, and the like and wherein alkyl is defined in B herein; wherein substituted alkyl is defined in C herein; wherein alkenyl is defined in D herein; wherein substituted alkenyl is defined in E herein; wherein alkynyl is defined in U herein; wherein substituted alkynyl is defined in Q<sup>231</sup> herein; wherein cycloalkyl is defined in F herein; wherein substituted cycloalkyl is defined in G herein; wherein aryl is defined in J herein; wherein substituted aryl is defined in K herein; wherein heteroaryl is defined in L herein; wherein substituted heteroaryl is defined in M herein; wherein heterocyclic is defined in N herein; and wherein substituted heterocyclic is defined in O herein;
- (D<sup>2</sup>) aminosulfonyloxy having the formula -NRSO<sub>2</sub>O-alkyl, -NRSO<sub>2</sub>O-substituted alkyl, -NRSO<sub>2</sub>O-alkenyl, -NRSO<sub>2</sub>O-substituted alkenyl, -NRSO<sub>2</sub>O-alkynyl, -NRSO<sub>2</sub>O-substituted alkynyl, -NRSO<sub>2</sub>O-cycloalkyl, -NRSO<sub>2</sub>O-substituted cycloalkyl, -NRSO<sub>2</sub>O-aryl, -NRSO<sub>2</sub>O-substituted aryl, -NRSO<sub>2</sub>O-heteroaryl, -NRSO<sub>2</sub>O-substituted heteroaryl, -NRSO<sub>2</sub>O-heterocyclic, and -NRSO<sub>2</sub>O-substituted heterocyclic where R is hydrogen or alkyl and wherein alkyl is defined

- in B herein; wherein substituted alkyl is defined in C herein; wherein alkenyl is defined in D herein; wherein substituted alkenyl is defined in E herein; wherein alkynyl is defined in U herein; wherein substituted alkynyl is defined in Q<sup>2</sup>31 herein; wherein cycloalkyl is defined in F herein; wherein substituted cycloalkyl is defined in G herein; wherein aryl is defined in J herein; wherein substituted aryl is defined in K herein; wherein heteroaryl is defined in L herein; wherein substituted heteroaryl is defined in M herein; wherein heterocyclic is defined in N herein; and wherein substituted heterocyclic is defined in O herein;
- (E<sup>2</sup>) aminosulfonyl having the formula -NRSO<sub>2</sub>alkyl, -NRSO<sub>2</sub>substituted alkyl, -NRSO<sub>2</sub>cycloalkyl, -NRSO<sub>2</sub>substituted cycloalkyl, -NRSO<sub>2</sub>alkenyl, -NRSO<sub>2</sub>substituted alkenyl, -NRSO<sub>2</sub>alkynyl, -NRSO<sub>2</sub>substituted alkynyl, -NRSO<sub>2</sub>aryl, -NRSO<sub>2</sub>substituted aryl, -NRSO<sub>2</sub>heteroaryl, -NRSO<sub>2</sub>substituted heteroaryl, -NRSO<sub>2</sub>heterocyclic, and -NRSO<sub>2</sub>substituted heterocyclic where R is hydrogen or alkyl and wherein alkyl is defined in B herein; wherein substituted alkyl is defined in C herein; wherein alkenyl is defined in D herein; wherein substituted alkenyl is defined in E herein; wherein alkynyl is defined in U herein; wherein substituted alkynyl is defined in Q<sup>2</sup>31 herein; wherein cycloalkyl is defined in F herein; wherein substituted cycloalkyl is defined in G herein; wherein aryl is defined in J herein; wherein substituted aryl is defined in K herein; wherein heteroaryl is defined in L herein; wherein substituted heteroaryl is defined in M herein; wherein heterocyclic is defined in N herein; and wherein substituted heterocyclic is defined in O herein;
- (F<sup>2</sup>) oxysulfonylamino having the formula -OSO<sub>2</sub>NH<sub>2</sub>, -OSO<sub>2</sub>NRR, -OSO<sub>2</sub>NR-alkyl, -OSO<sub>2</sub>NR-substituted alkyl, -OSO<sub>2</sub>NR-alkenyl, -OSO<sub>2</sub>NR-substituted alkenyl, -OSO<sub>2</sub>NR-alkynyl, -OSO<sub>2</sub>NR-substituted

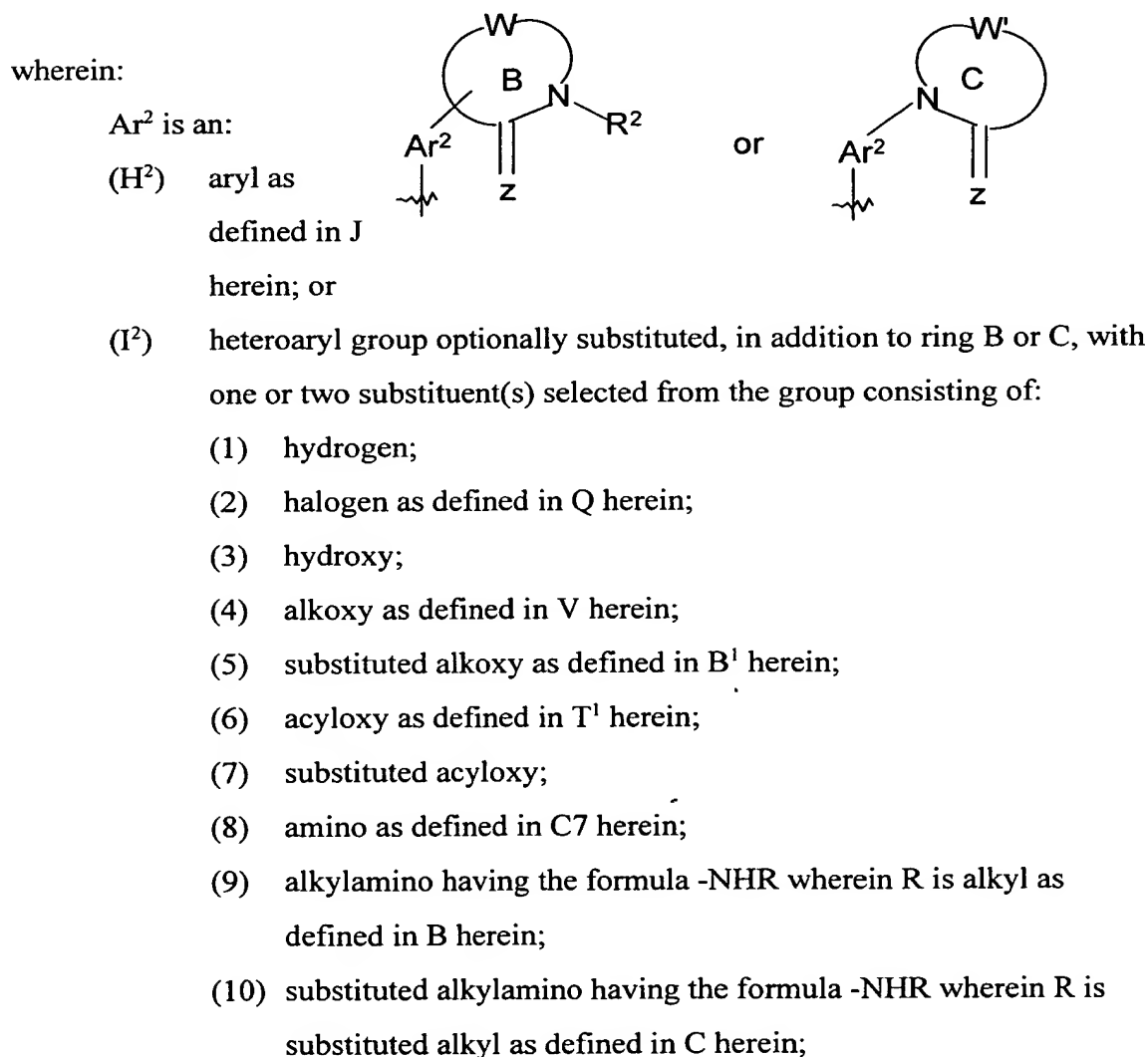
alkynyl, -OSO<sub>2</sub>NR-cycloalkyl, -OSO<sub>2</sub>NR-substituted cycloalkyl, -OSO<sub>2</sub>NR-aryl, -OSO<sub>2</sub>NR-substituted aryl, -OSO<sub>2</sub>NR-heteroaryl, -OSO<sub>2</sub>NR-substituted heteroaryl, -OSO<sub>2</sub>NR-heterocyclic, and -OSO<sub>2</sub>NR-substituted heterocyclic where R is hydrogen, alkyl or where each R is joined to form, together with the nitrogen atom a heterocyclic or substituted heterocyclic ring and wherein alkyl is defined in B herein; wherein substituted alkyl is defined in C herein; wherein alkenyl is defined in D herein; wherein substituted alkenyl is defined in E herein; wherein alkynyl is defined in U herein; wherein substituted alkynyl is defined in Q<sup>231</sup> herein; wherein cycloalkyl is defined in F herein; wherein substituted cycloalkyl is defined in G herein; wherein aryl is defined in J herein; wherein substituted aryl is defined in K herein; wherein heteroaryl is defined in L herein; wherein substituted heteroaryl is defined in M herein; wherein heterocyclic is defined in N herein; and wherein substituted heterocyclic is defined in O herein; and

(G<sup>2</sup>) oxysulfonyl selected from the groups alkyl-SO<sub>2</sub>O-, substituted alkyl-SO<sub>2</sub>O-, alkenyl-SO<sub>2</sub>O-, substituted alkenyl-SO<sub>2</sub>O-, alkynyl-SO<sub>2</sub>O-, substituted alkynyl-SO<sub>2</sub>O-, aryl-SO<sub>2</sub>O-, substituted aryl-SO<sub>2</sub>O-, cycloalkyl-SO<sub>2</sub>O-, substituted cycloalkyl-SO<sub>2</sub>O-, heteroaryl-SO<sub>2</sub>O-, substituted heteroaryl-SO<sub>2</sub>O-, heterocyclic-SO<sub>2</sub>O-, and substituted heterocyclic-SO<sub>2</sub>O- wherein alkyl is defined in B herein; wherein substituted alkyl is defined in C herein; wherein alkenyl is defined in D herein; wherein substituted alkenyl is defined in E herein; wherein alkynyl is defined in U herein; wherein substituted alkynyl is defined in Q<sup>231</sup> herein; wherein cycloalkyl is defined in F herein; wherein substituted cycloalkyl is defined in G herein; wherein aryl is defined in J herein; wherein substituted aryl is defined in K herein; wherein heteroaryl is defined in L herein; wherein substituted heteroaryl is

defined in M herein; wherein heterocyclic is defined in N herein; and  
wherein substituted heterocyclic is defined in O herein;

provided that when R<sup>9</sup> is acylamino or acyloxy then the acylamino or acyloxy group does not carry an aryl, substituted aryl, heteroaryl or substituted heteroaryl group; or

(ii) a group of formula (a) or (b):



- (11) dialkylamino having the formula -NRR wherein each R is alkyl as defined in B herein;
- (12) substituted dialkylamino having the formula -NRR wherein each R is substituted alkyl as defined in C herein;
- (13) acylamino as defined in S<sup>1</sup> herein;
- (14) substituted acylamino;
- (15) N-acyl-N-alkylamino wherein acyl is defined in R<sup>1</sup> herein and alkylamino is defined in I<sup>2</sup>9 herein;
- (16) substituted N-acyl-N-alkylamino wherein acyl is defined in R<sup>1</sup> herein and substituted alkylamino is defined in I<sup>2</sup>10 herein;
- (17) (alkylsulfonyl)amino wherein alkylsulfonyl is defined in C<sup>3</sup> herein and amino is defined in C7 herein;
- (18) substituted (alkylsulfonyl)amino wherein substituted alkylsulfonyl is defined in D<sup>3</sup> herein and amino is defined in C7 herein;
- (19) N-(alkylsulfonyl)-N-alkylamino wherein alkylsulfonyl is defined in C<sup>3</sup> herein and alkylamino is defined in I<sup>2</sup>9 herein;
- (20) substituted N-(alkylsulfonyl)-N-alkylamino wherein substituted alkylsulfonyl is defined in D<sup>3</sup> herein and substituted alkylamino is defined in I<sup>2</sup>10 herein;
- (21) alkyl as defined in B herein;
- (22) substituted alkyl as defined in C herein;
- (23) cycloalkyl as defined in F herein;
- (24) substituted cycloalkyl as defined in G herein;
- (25) alkenyl as defined in D herein;
- (26) substituted alkenyl as defined in E herein;
- (27) cycloalkenyl as defined in H herein;
- (28) substituted cycloalkenyl as defined in I herein;

- (29) alkynyl as defined in U herein;
- (30) substituted alkynyl as defined in Q<sup>231</sup> herein;
- (31) cyano;
- (32) acyl as defined in R<sup>1</sup> herein;
- (33) substituted acyl;
- (34) carboxy;
- (35) substituted carboxy;
- (36) thiol as defined in X<sup>2</sup> herein;
- (37) alkylthio as defined in X herein;
- (38) substituted alkylthio as defined in Z<sup>2</sup> herein;
- (39) alkylsulfoxy as defined in A<sup>3</sup> herein;
- (40) substituted alkylsulfoxy as defined in B<sup>3</sup> herein;
- (41) alkylsulfonyl as defined in C<sup>3</sup> herein; and
- (42) substituted alkylsulfonyl as defined in D<sup>3</sup> herein;

Z is -O- or -S-;

B is a group wherein W, together with -C(=Z)NR<sup>2</sup>-, forms a saturated or unsaturated heterocyclic group, wherein heterocyclic is defined in N herein, containing 2 to 5 carbon atoms and 0 to 4 additional heteroatoms selected from the group consisting of:

- (J<sup>2</sup>) nitrogen;
- (K<sup>2</sup>) oxygen; and
- (L<sup>2</sup>) -So<sub>n</sub>- (where n is 0 to 2);

wherein said saturated or unsaturated heterocyclic group is optionally fused with one or two ring(s) structures selected from the group consisting of:

- (M<sup>2</sup>) cycloalkyl as defined in F herein;
- (N<sup>2</sup>) cycloalkenyl as defined in H herein;
- (O<sup>2</sup>) heterocyclic as defined in N herein;
- (P<sup>2</sup>) aryl as defined in J herein; and



(Q<sup>2</sup>) heteroaryl group, wherein heteroaryl is as defined in L herein, to form a bi- or tri-fused ring system and further wherein said heterocyclic group and each of such ring structures are optionally substituted with 1 to 3 substituents selected from the group consisting of with one or two substituent(s) selected from the group consisting of:

- (1) hydrogen;
- (2) halogen as defined in Q herein;
- (3) hydroxy;
- (4) alkoxy as defined in V herein;
- (5) substituted alkoxy as defined in B<sup>1</sup> herein;
- (6) acyloxy as defined in T<sup>1</sup> herein;
- (7) substituted acyloxy;
- (8) amino as defined in C7 herein;
- (9) alkylamino as defined in I<sup>2</sup>9 herein;
- (10) substituted alkylamino as defined in I<sup>2</sup>10 herein;
- (11) dialkylamino as defined in I<sup>2</sup>11 herein;
- (12) substituted dialkylamino as defined in I<sup>2</sup>12 herein;
- (13) acylamino as defined in S<sup>1</sup> herein;
- (14) substituted acylamino;
- (15) N-acyl-N-alkylamino wherein acyl is defined in R<sup>1</sup> herein and alkylamino I<sup>2</sup>9 herein;
- (16) substituted N-acyl-N-alkylamino wherein acyl is defined in R<sup>1</sup> herein and substituted alkylamino is defined in I<sup>2</sup>10 herein;
- (17) alkylene dioxy;
- (18) (alkylsulfonyl)amino wherein alkylsulfonyl is defined in C<sup>3</sup> herein and amino is define in C7 herein;

- (19) substituted (alkylsulfonyl)amino wherein substituted alkylsulfonyl is defined in D<sup>3</sup> herein and amino is defined in C7 herein;
- (20) N-(alkylsulfonyl)-N-alkylamino wherein alkylsulfonyl is defined in C<sup>3</sup> herein and alkylamino is defined in I<sup>29</sup> herein;
- (21) substituted N-(alkylsulfonyl)-N-alkylamino wherein substituted alkylsulfonyl is defined in D<sup>3</sup> herein and substituted alkylamino is defined in I<sup>210</sup> herein;
- (22) alkyl as defined in B herein;
- (23) substituted alkyl as defined in C herein;
- (24) cycloalkyl as defined in F herein;
- (25) substituted cycloalkyl as defined in G herein;
- (26) alkenyl as defined in D herein;
- (27) substituted alkenyl as defined in E herein;
- (28) cycloalkenyl as defined in H herein;
- (29) substituted cycloalkenyl as defined in I herein;
- (30) alkynyl as defined in U herein;
- (31) substituted alkynyl having from 1 to 5 substituents selected from the group consisting of:
  - (a) alkoxy as defined in V herein;
  - (b) substituted alkoxy as defined in B<sup>1</sup> herein;
  - (c) acyl as defined in R<sup>1</sup> herein;
  - (d) acylamino as defined in S<sup>1</sup> herein;
  - (e) thiocarbonylamino as defined in B<sup>2</sup> herein;
  - (f) acyloxy as defined in T<sup>1</sup> herein;
  - (g) amino as defined in C7 herein;
  - (h) amidino as defined in C8 herein;

- (i) alkylamidino wherein alkyl is defined in B herein and amidino is defined in C8 herein;
- (j) thioamidino as defined in A<sup>2</sup> herein;
- (k) aminoacyl as defined in U<sup>1</sup> herein;
- (l) aminocarbonylamino as defined in V<sup>1</sup> herein;
- (m) aminothiocabonylamino as defined in W<sup>1</sup> herein;
- (n) aminocarbonyloxy as defined in X<sup>1</sup> herein;
- (o) aryl as defined in J herein;
- (p) substituted aryl as defined in K herein;
- (q) aryloxy as defined in I<sup>1</sup> herein;
- (r) substituted aryloxy as defined in J<sup>1</sup> herein;
- (s) aryloxyaryl as defined in C19 herein;
- (t) substituted aryloxyaryl as defined in C20 herein;
- (u) halogen as defined in Q herein;
- (v) hydroxyl;
- (w) cyano;
- (x) nitro;
- (y) carboxyl;
- (z) carboxylalkyl wherein alkyl is defined in B herein;
- (a<sup>1</sup>) carboxyl-substituted alkyl wherein substituted alkyl is defined in C herein;
- (b<sup>1</sup>) carboxyl-cycloalkyl wherein cycloalkyl is defined in F herein;
- (c<sup>1</sup>) carboxyl-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
- (d<sup>1</sup>) carboxylaryl wherein aryl is defined in J herein;
- (e<sup>1</sup>) carboxyl-substituted aryl wherein substituted aryl is defined in K herein;

- (f<sup>1</sup>) carboxylheteroaryl wherein heteroaryl is defined in L herein;
- (g<sup>1</sup>) carboxyl-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (h<sup>1</sup>) carboxylheterocyclic wherein heterocyclic is defined in N herein;
- (i<sup>1</sup>) carboxyl-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (j<sup>1</sup>) cycloalkyl as defined in F herein;
- (k<sup>1</sup>) substituted cycloalkyl as defined in G herein;
- (l<sup>1</sup>) guanidino as defined in C38 herein;
- (m<sup>1</sup>) guanidinosulfone as defined in C39 herein;
- (n<sup>1</sup>) thiol as defined in X<sup>2</sup> herein;
- (o<sup>1</sup>) thioalkyl as defined in X herein;
- (p<sup>1</sup>) substituted thioalkyl as defined in C42 herein;
- (q<sup>1</sup>) thioaryl as defined in C43 herein;
- (r<sup>1</sup>) substituted thioaryl as defined in C44 herein;
- (s<sup>1</sup>) thiocycloalkyl as defined in C45 herein;
- (t<sup>1</sup>) substituted thiocycloalkyl as defined in C46 herein;
- (u<sup>1</sup>) thioheteroaryl as defined in C47 herein;
- (v<sup>1</sup>) substituted thioheteroaryl as defined in C48 herein;
- (w<sup>1</sup>) thioheterocyclic as defined in C49 herein;
- (x<sup>1</sup>) substituted thioheterocyclic as defined in C50 herein;
- (y<sup>1</sup>) heteroaryl as defined in L herein;
- (z<sup>1</sup>) substituted heteroaryl as defined in M herein;
- (a<sup>2</sup>) heterocyclic as defined in N herein;
- (b<sup>2</sup>) substituted heterocyclic as defined in O herein;
- (c<sup>2</sup>) cycloalkoxy as defined in E<sup>1</sup> herein;

- (d<sup>2</sup>) substituted cycloalkoxy as defined in F<sup>1</sup> herein;
- (e<sup>2</sup>) heteroaryloxy as defined in K<sup>1</sup> herein;
- (f<sup>2</sup>) substituted heteroaryloxy as defined in L<sup>1</sup> herein;
- (g<sup>2</sup>) heterocyclyloxy as defined in M<sup>1</sup> herein;
- (h<sup>2</sup>) substituted heterocyclyloxy as defined in N<sup>1</sup> herein;
- (i<sup>2</sup>) oxycarbonylamino as defined in Y<sup>1</sup> herein;
- (j<sup>2</sup>) oxythiocarbonylamino as defined in Z<sup>1</sup> herein;
- (k<sup>2</sup>) -OS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (l<sup>2</sup>) -OS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (m<sup>2</sup>) -OS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;
- (n<sup>2</sup>) -OS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (o<sup>2</sup>) -OS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (p<sup>2</sup>) -OS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (q<sup>2</sup>) -OS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (r<sup>2</sup>) -OS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (s<sup>2</sup>) -OSO<sub>2</sub>-NRR where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;
- (t<sup>2</sup>) -NRS(O)<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
- (u<sup>2</sup>) -NRS(O)<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
- (v<sup>2</sup>) -NRS(O)<sub>2</sub>-aryl wherein aryl is defined in J herein;

- (w<sup>2</sup>) -NRS(O)<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
- (x<sup>2</sup>) -NRS(O)<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;
- (y<sup>2</sup>) -NRS(O)<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (z<sup>2</sup>) -NRS(O)<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
- (a<sup>3</sup>) -NRS(O)<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein;
- (b<sup>3</sup>) -NRS(O)<sub>2</sub>-NR-alkyl wherein alkyl is defined in B herein;
- (c<sup>3</sup>) -NRS(O)<sub>2</sub>-NR-substituted alkyl wherein substituted alkyl is defined in C herein;
- (d<sup>3</sup>) -NRS(O)<sub>2</sub>-NR-aryl wherein aryl is defined in J herein;
- (e<sup>3</sup>) -NRS(O)<sub>2</sub>-NR-substituted aryl wherein substituted aryl is defined in K herein;
- (f<sup>3</sup>) -NRS(O)<sub>2</sub>-NR-heteroaryl wherein heteroaryl is defined in L herein;
- (g<sup>3</sup>) -NRS(O)<sub>2</sub>-NR-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
- (h<sup>3</sup>) -NRS(O)<sub>2</sub>-NR-heterocyclic wherein heterocyclic is defined in N herein;
- (i<sup>3</sup>) -NRS(O)<sub>2</sub>-NR-substituted heterocyclic wherein substituted heterocyclic is defined in O herein and where R is:
  - (a) hydrogen; or
  - (b) alkyl as defined in B herein;

- (j<sup>3</sup>) mono- and di-alkylamino wherein alkylamino is defined in I<sup>29</sup> herein;
- (k<sup>3</sup>) mono- and di-(substituted alkyl)amino wherein substituted alkyl is defined in C herein and amino is defined in C7 herein;
- (l<sup>3</sup>) mono- and di-arylamino wherein aryl is defined in J herein and amino is defined in C7 herein;
- (m<sup>3</sup>) mono- and di-substituted arylamino wherein substituted aryl is defined in K herein and amino is defined in C7 herein;
- (n<sup>3</sup>) mono- and di-heteroarylamino wherein heteroaryl is defined in L herein and amino is defined in C7 herein;
- (o<sup>3</sup>) mono- and di-substituted heteroarylamino wherein substituted heteroaryl is defined in M herein and amino is defined in C7 herein;
- (p<sup>3</sup>) mono- and di-heterocyclic amino wherein heterocyclic is defined in N herein and amino is defined in C7 herein;
- (q<sup>3</sup>) mono- and di-substituted heterocyclic amino wherein substituted heterocyclic is defined in O herein and amino is defined in C7 herein;
- (r<sup>3</sup>) unsymmetric di-substituted amines having different substituents selected from:
  - (a) alkyl as defined in B herein;
  - (b) substituted alkyl as defined in C herein;
  - (c) aryl as defined in J herein;
  - (d) substituted aryl as defined in K herein;
  - (e) heteroaryl as defined in L herein;

- (f) substituted heteroaryl as defined in M herein;
- (g) heterocyclic as defined in N herein; and
- (h) substituted heterocyclic as defined in O herein and substituted alkynyl groups having amino groups blocked by conventional blocking groups such as Boc, Cbz, formyl, and the like or alkynyl/substituted alkynyl groups substituted with:
  - (i) -SO<sub>2</sub>-alkyl wherein alkyl is defined in B herein;
  - (ii) -SO<sub>2</sub>-substituted alkyl wherein substituted alkyl is defined in C herein;
  - (iii) -SO<sub>2</sub>-alkenyl wherein alkenyl is defined in D herein;
  - (iv) -SO<sub>2</sub>-substituted alkenyl wherein substituted alkenyl is defined in E herein;
  - (v) -SO<sub>2</sub>-cycloalkyl wherein cycloalkyl is defined in F herein;
  - (vi) -SO<sub>2</sub>-substituted cycloalkyl wherein substituted cycloalkyl is defined in G herein;
  - (vii) -SO<sub>2</sub>-aryl wherein aryl is defined in J herein;
  - (viii) -SO<sub>2</sub>-substituted aryl wherein substituted aryl is defined in K herein;
  - (ix) -SO<sub>2</sub>-heteroaryl wherein heteroaryl is defined in L herein;



- (x) -SO<sub>2</sub>-substituted heteroaryl wherein substituted heteroaryl is defined in M herein;
  - (xi) -SO<sub>2</sub>-heterocyclic wherein heterocyclic is defined in N herein;
  - (xii) -SO<sub>2</sub>-substituted heterocyclic wherein substituted heterocyclic is defined in O herein; and
  - (xiii) -SO<sub>2</sub>NRR where R is:
    - (a) hydrogen; or
    - (b) alkyl as defined in B herein;
- 
- (R<sup>2</sup>) cyano;
  - (S<sup>2</sup>) acyl as defined in R<sup>1</sup> herein;
  - (T<sup>2</sup>) substituted acyl;
  - (U<sup>2</sup>) carboxy;
  - (V<sup>2</sup>) substituted carboxy;
  - (W<sup>2</sup>) nitro;
  - (X<sup>2</sup>) thiol having the formula "-SH";
  - (Y<sup>2</sup>) alkylthio as defined in X herein;
  - (Z<sup>2</sup>) substituted alkylthio having the formula "-S-substituted alkyl";
  - (A<sup>3</sup>) alkylsulfoxy having the formula "-SO-alkyl";
  - (B<sup>3</sup>) substituted alkylsulfoxy having the formula "-SO-substituted alkyl";
  - (C<sup>3</sup>) alkylsulfonyl having the formula "-SO<sub>2</sub>-alkyl";
  - (D<sup>3</sup>) substituted alkylsulfonyl having the formula "-SO<sub>2</sub>-substituted alkyl";
  - (E<sup>3</sup>) aryl as defined in J herein;
  - (F<sup>3</sup>) substituted aryl as defined in K herein;
  - (G<sup>3</sup>) heteroaryl as defined in L herein; and
  - (H<sup>3</sup>) substituted heteroaryl as defined in M herein;

R<sup>2</sup> is selected from the group consisting of:

- (I<sup>3</sup>) alkyl as defined in B herein;
- (J<sup>3</sup>) substituted alkyl as defined in C herein;
- (K<sup>3</sup>) aryl as defined in J herein;
- (L<sup>3</sup>) substituted aryl as defined in K herein;
- (M<sup>3</sup>) heteroaryl as defined in L herein;
- (N<sup>3</sup>) substituted heteroaryl as defined in M herein;
- (O<sup>3</sup>) cycloalkyl as defined in F herein;
- (P<sup>3</sup>) substituted cycloalkyl as defined in G herein;
- (Q<sup>3</sup>) cycloalkenyl as defined in H herein; and
- (R<sup>3</sup>) substituted cycloalkenyl as defined in I herein;

C is a group wherein W', together with -C(=Z)N-, forms a saturated or unsaturated heterocyclic group containing 2 to 5 carbon atoms and 0 to 4 additional heteroatoms selected from the group consisting of:

- (S<sup>3</sup>) nitrogen;
- (T<sup>3</sup>) oxygen; and
- (U<sup>3</sup>) -S<sub>n</sub>- (where n is 0 to 2);

wherein said saturated or unsaturated heterocyclic group is optionally fused with one or two ring(s) structures selected from the group consisting of:

- (V<sup>3</sup>) cycloalkyl as defined in F herein;
- (W<sup>3</sup>) cycloalkenyl as defined in H herein;
- (X<sup>3</sup>) heterocyclic as defined in N herein;
- (Y<sup>3</sup>) aryl as defined in J herein; and
- (Z<sup>3</sup>) heteroaryl group, wherein heteroaryl is defined in L herein, to form a bi- or tri-fused ring system and further wherein said heterocyclic group and each of such ring structures are optionally substituted with 1 to 3 substituents selected from the group consisting of with one or two substituent(s) selected from the group consisting of:

- (1) hydrogen;
- (2) halogen as defined in Q herein;
- (3) hydroxy;
- (4) alkoxy as defined in V herein;
- (5) substituted alkoxy as defined in B<sup>1</sup> herein;
- (6) alkylendioxy;
- (7) acyloxy as defined in T<sup>1</sup> herein;
- (8) substituted acyloxy;
- (9) amino as defined in C7 herein;
- (10) alkylamino as defined in I<sup>2</sup>9 herein;
- (11) substituted alkylamino as defined in I<sup>2</sup>10 herein;
- (12) dialkylamino as defined in I<sup>2</sup>11 herein;
- (13) substituted dialkylamino as defined in I<sup>2</sup>12 herein;
- (14) acylamino as defined in S<sup>1</sup> herein;
- (15) substituted acylamino;
- (16) N-acyl-N-alkylamino wherein acyl is defined in R<sup>1</sup> herein and alkylamino I<sup>2</sup>9 herein;
- (17) substituted N-acyl-N-alkylamino wherein acyl is defined in R<sup>1</sup> herein and substituted alkylamino is defined in I<sup>2</sup>10 herein;
- (18) (alkylsulfonyl)amino wherein alkylsulfonyl is defined in C<sup>3</sup> herein and amino is defined in C7 herein;
- (19) substituted (alkylsulfonyl)amino wherein substituted alkylsulfonyl is defined in D<sup>3</sup> herein and amino is defined in C7 herein;
- (20) N-(alkylsulfonyl)-N-alkylamino wherein alkylsulfonyl is defined in C<sup>3</sup> herein and alkylamino is defined in I<sup>2</sup>9 herein;

- (21) substituted N-(alkylsulfonyl)-N-alkylamino wherein substituted alkylsulfonyl is defined in D<sup>3</sup> herein and substituted alkylamino is defined in I<sup>2</sup>10 herein;
- (22) alkyl as defined in B herein;
- (23) substituted alkyl as defined in C herein;
- (24) cycloalkyl as defined in F herein;
- (25) substituted cycloalkyl as defined in G herein;
- (26) alkenyl as defined in D herein;
- (27) substituted alkenyl as defined in E herein;
- (28) cycloalkenyl as defined in H herein;
- (29) substituted cycloalkenyl as defined in I herein;
- (30) alkynyl as defined in U herein;
- (31) substituted alkynyl as defined in Q<sup>2</sup>31 herein;
- (32) cyano;
- (33) nitro;
- (34) acyl as defined in R<sup>1</sup> herein;
- (35) substituted acyl;
- (36) carboxy;
- (37) substituted carboxy;
- (38) thiol as defined in X<sup>2</sup> herein;
- (39) alkylthio as defined in X herein;
- (40) substituted alkylthio as defined in Z<sup>2</sup> herein;
- (41) alkylsulfoxy as defined in A<sup>3</sup> herein;
- (42) substituted alkylsulfoxy as defined in B<sup>3</sup> herein;
- (43) alkylsulfonyl as defined in C<sup>3</sup> herein;
- (44) substituted alkylsulfonyl as defined in D<sup>3</sup> herein;
- (45) aryl as defined in J herein;
- (46) substituted aryl as defined in K herein;

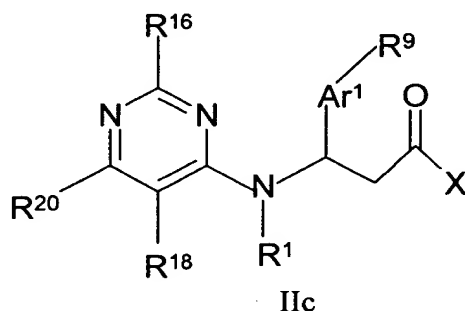
- (47) heteroaryl as defined in L herein; and
  - (48) substituted heteroaryl as defined in M herein; or
- (iii) HetAr where HetAr is a:
- (A<sup>4</sup>) nitrogen containing heteroaryl, having a heteroaryl ring that contains at least one nitrogen atom in the ring, and that is optionally substituted with:
    - (1) aryl as defined in J herein; or
    - (2) substituted aryl group, wherein substituted aryl is defined in K herein;

or enantiomers, diastereomers or pharmaceutically acceptable salts thereof;  
and further wherein the compound of Formula I has a binding affinity to VLA-4 as expressed by an IC<sub>50</sub> of 15  $\mu$ M or less.

(New) The compound of Claim 27 wherein R<sup>2a</sup> is an -Ar<sup>1</sup>-R<sup>9</sup> group wherein Ar<sup>1</sup> and R<sup>9</sup> are as defined in Claim 27.

- 28. The compound of Claim 28 wherein Ar<sup>1</sup> is phenyl with the R<sup>9</sup> in the *para* position of the phenyl ring.
- 29. The compound of Claim 29 wherein R<sup>9</sup> is selected from the group consisting of -O-Z<sup>a</sup>-NR<sup>11</sup>R<sup>11'</sup> and -O-Z<sup>a</sup>-R<sup>12</sup> wherein R<sup>11</sup> and R<sup>11'</sup> are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, and where R<sup>11</sup> and R<sup>11'</sup> are joined to form a heterocycle or a substituted heterocycle, R<sup>12</sup> is selected from the group consisting of heterocycle and substituted heterocycle, and Z<sup>a</sup> is selected from the group consisting of -C(O)- and -SO<sub>2</sub>-.

30. The compound of Claim 30 wherein  $R^9$  is  $-\text{OC}(\text{O})\text{NR}^{11}\text{R}^{11}$ .
31. The compound of Claim 31 wherein  $\text{Ar}^1$  is phenyl with a  $-\text{OCON}(\text{CH}_3)_2$  group at the para position of the phenyl ring.
32. The compound of Claims 27-32 wherein  $R^1$ ,  $R^3$  and  $R^{3a}$  are hydrogen, and X is hydroxyl.
33. The compound of Claim 27 wherein the compound has formula IIc:



wherein X is hydroxy or alkoxy;

$R^1$  is hydrogen;

$R^{16}$  is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen; and

$R^{18}$  is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R<sup>20</sup> is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

Ar<sup>1</sup> is aryl or heteroaryl optionally substituted with one or two substituents selected from the group consisting of hydroxy, acyl, acylamino, acyloxy, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, aminoacyl, aminocarbonyloxy, carboxyl, carboxylalkyl, carboxylamido, cyano, thiol, thioalkyl, substituted thioalkyl, halo, nitro provided that said acyl, acylamino, acyloxy, substituted alkyl, substituted alkoxy and substituted thioalkyl do not carry an aryl, substituted aryl, heteroaryl or substituted heteroaryl group; and

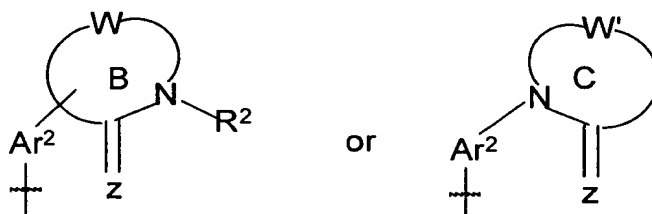
R<sup>9</sup> is selected from the group consisting of acyl, acylamino, acyloxy, aminoacyl, aminocarbonylamino, aminothiocabonylamino, aminocarbonyloxy, oxycarbonylamino, oxythiocarbonylamino, thioamidino, thiocarbonylamino, aminosulfonylamino, aminosulfonyloxy, aminosulfonyl, oxysulfonylamino and oxysulfonyl provided that when R<sup>9</sup> is acylamino or acyloxy then the acylamino or acyloxy group does not carry an aryl, substituted aryl, heteroaryl or substituted heteroaryl group;

or enantiomers, diastereomers or pharmaceutically acceptable salts thereof.

34. The compound of Claim 34 wherein Ar<sup>1</sup> is phenyl, pyridinyl, or pyrimidinyl ring.
35. The compound of Claim 35 wherein R<sup>9</sup> is selected from the group consisting of -O-Z<sup>a</sup>-NR<sup>11</sup>R<sup>11'</sup> and -O-Z<sup>a</sup>-R<sup>12</sup> wherein R<sup>11</sup> and R<sup>11'</sup> are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, and where R<sup>11</sup> and R<sup>11'</sup> are joined to form a heterocycle or a substituted heterocycle, R<sup>12</sup> is selected from the group

consisting of heterocycle and substituted heterocycle, and  $Z^a$  is selected from the group consisting of  $-C(O)-$  and  $-SO_2-$ .

36. The compound of Claim 36 wherein  $R^9$  is  $-OC(O)NR^{11}R^{11'}$ .
37. The compound of Claim 37 wherein X is hydroxy and  $R^1$ ,  $R^3$  and  $R^{3a}$  are hydrogen and  $R^9$  is  $-OCON(CH_3)_2$ .
38. The compound of Claim 27 wherein  $R^{2a}$  is a group of formula (a) or (b):



wherein  $Ar^2$ , B, C and Z are as defined in Claim 27.

39. The compound of Claim 39 wherein B is selected from the group wherein:
- (a) W, together with  $-C(=Z)NR^2-$  where Z is  $-O-$ , forms an unsaturated heterocyclic group containing 3 or 4 carbon atoms and 0 or 1 additional nitrogen atoms and further the wherein the unsaturated heterocyclic group is optionally substituted, in addition to the  $R^2$  group, with 1 or 2 substituents selected from the group consisting of alkyl, alkoxy, substituted alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or dialkylamino; or
- (b) W, together with  $-C(=Z)NR^2-$  where Z is  $-O-$ , forms a saturated or unsaturated heterocyclic group containing 3 or 4 carbon atoms and 0 or 1 additional nitrogen atoms wherein said saturated or unsaturated heterocyclic group is fused to a heterocyclic ring selected from the group consisting of dioxolane, dioxane,



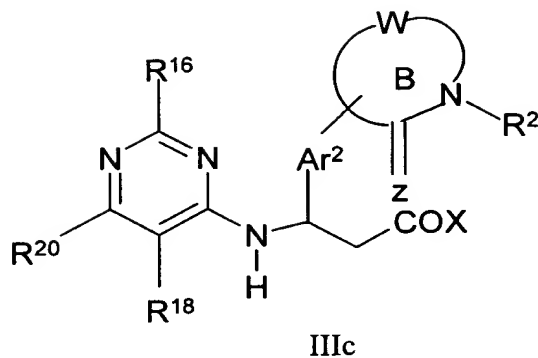
homodioxane, oxetane, tetrahydrofuran, dihydropyran, furan, oxazolidine, oxazole, isoxazole, oxazolidinone, oxathiolane, and 1,3-dioxolan-2-one and wherein the resulting fused ring is optionally substituted, in addition to the  $R^2$  group, on any ring atom capable of substitution with 1 or 2 substituents selected from the group consisting of alkyl, alkoxy, substituted alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or dialkylamino; and

C is either a group wherein:

- (a) W, together with  $-C(=Z)NR^2$ - where Z is -O-, forms an unsaturated heterocyclic group containing 2 to 4 carbon atoms and 0 to 2 additional nitrogen atoms and further the wherein the unsaturated heterocyclic group is optionally substituted, in addition to the  $R^2$  group, with 1 or 2 substituents selected from the group consisting of alkyl, alkoxy, substituted alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or dialkylamino; or
- (b) W, together with  $-C(=Z)NR^2$ - where Z is -O-, forms a saturated or unsaturated heterocyclic group containing 2 to 4 carbon atoms and 0 to 2 additional nitrogen atoms wherein said saturated or unsaturated heterocyclic group is fused to a heterocyclic ring selected from the group consisting of dioxolane, dioxane, homodioxane, oxetane, tetrahydrofuran, dihydropyran, furan, oxazolidine, oxazole, isoxazole, oxazolidinone, oxathiolane, and 1,3-dioxolan-2-one and wherein the resulting fused ring is optionally substituted, in addition to the  $R^2$  group, on any ring atom capable of substitution with 1 or 2 substituents selected from the group consisting of alkyl, alkoxy, substituted alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or dialkylamino.

40. The compound of Claim 40 wherein  $R^1$ ,  $R^3$  and  $R^{3a}$  are hydrogen, and X is preferably hydroxy.

41. The compound of Claim 27 wherein the compound has the formula IIIc:



wherein:

X is hydroxyl or alkoxy;

Ar<sup>2</sup> is an aryl or heteroaryl group optionally substituted, in addition to ring B or C, with one or two substituent(s) selected from the group consisting of hydrogen, halogen, hydroxy, alkoxy, substituted alkoxy, acyloxy, substituted acyloxy, amino, alkylamino, substituted alkylamino, dialkylamino, substituted dialkylamino, acylamino, substituted acylamino, N-acyl-N-alkylamino, substituted N-acyl-N-alkylamino, (alkylsulfonyl)amino, substituted (alkylsulfonyl)amino, N-(alkylsulfonyl)-N-alkylamino, substituted N-(alkylsulfonyl)-N-alkylamino, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, cyano, acyl, substituted acyl, carboxy, substituted carboxy, thiol, alkylthio, substituted alkylthio, alkylsulfoxy, substituted alkylsulfoxy, alkylsulfonyl, and substituted alkylsulfonyl;

R<sup>16</sup> is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen; and

R<sup>18</sup> is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

$R^{20}$  is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

B is a group wherein W, together with  $-C(=Z)NR^2-$ , forms a saturated or unsaturated heterocyclic group containing 2 to 5 carbon atoms and 0 to 4 additional heteroatoms selected from the group consisting of nitrogen, oxygen, and  $-SO_n-$  (where n is 0 to 2) wherein said saturated or unsaturated heterocyclic group is optionally fused with one or two ring(s) structures selected from the group consisting of cycloalkyl, cycloalkenyl, heterocyclic, aryl and heteroaryl group to form a bi- or tri-fused ring system and further wherein said heterocyclic group and each of such ring structures are optionally substituted with 1 to 3 substituents selected from the group consisting of with one or two substituent(s) selected from the group consisting of hydrogen, halogen, hydroxy, alkoxy, substituted alkoxy, acyloxy, substituted acyloxy, amino, alkylamino, substituted alkylamino, dialkylamino, substituted dialkylamino, acylamino, substituted acylamino, N-acyl-N-alkylamino, substituted N-acyl-N-alkylamino, alkylenedioxy, (alkylsulfonyl)amino, substituted (alkylsulfonyl)amino, N-(alkylsulfonyl)-N-alkylamino, substituted N-(alkylsulfonyl)-N-alkylamino, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, cyano, acyl, substituted acyl, carboxy, substituted carboxy, nitro, thiol, alkylthio, substituted alkylthio, alkylsulfoxy, substituted alkylsulfoxy, alkylsulfonyl, substituted alkylsulfonyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl;

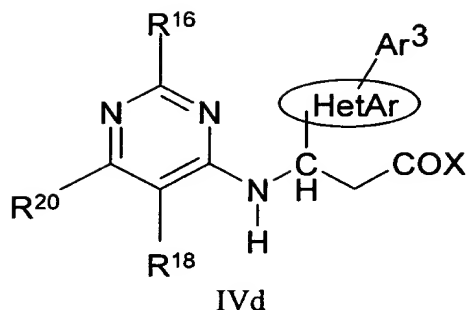
$R^2$  is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, and substituted cycloalkenyl;

or enantiomers, diastereomers or pharmaceutically acceptable salts thereof.

42. The compound of Claim 42 wherein B is either:

- (a) a group wherein W, together with  $-C(=Z)NR^2-$  where Z is -O-, forms an unsaturated heterocyclic group containing 2 to 4 carbon atoms and 0 to 2 additional nitrogen atoms and further the wherein the unsaturated heterocyclic group is optionally substituted, in addition to the  $R^2$  group, with 1 or 2 substituents selected from the group consisting of alkyl, alkoxy, substituted alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or dialkylamino; or
- (b) a group wherein W, together with  $-C(=Z)NR^2-$  where Z is -O-, forms a saturated or unsaturated heterocyclic group containing 2 to 4 carbon atoms and 0 to 2 additional nitrogen atoms wherein said saturated or unsaturated heterocyclic group is fused to a heterocyclic ring selected from the group consisting of dioxolane, dioxane, homodioxane, oxetane, tetrahydrofuran, dihydropyran, furan, oxazolidine, oxazole, isoxazole, oxazolidinone, oxathiolane, and 1,3-dioxolan-2-one and wherein the resulting fused ring is optionally substituted, in addition to the  $R^2$  group, on any ring atom capable of substitution with 1 or 2 substituents selected from the group consisting of alkyl, alkoxy, substituted alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or dialkylamino.

43. The compound of Claim 43 wherein  $Ar^2$  is phenyl.
44. The compound of Claim 27 wherein  $R^{2a}$  is HetAr where HetAr is a nitrogen containing 6- membered heteroaryl that is optionally substituted with an aryl or substituted aryl group.
45. The compound of Claim 27 wherein the compounds are of formula IVd:



wherein:

HetAr is a nitrogen containing heteroaryl group;

Ar<sup>3</sup> is aryl or substituted aryl;

R<sup>16</sup> is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen; and

R<sup>18</sup> is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R<sup>20</sup> is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

X is hydroxyl;

or enantiomers, diastereomers or pharmaceutically acceptable salts thereof.

46. The compound of Claim 46 wherein HetAr is pyridinyl, pyrimidinyl, pyrazinyl, or pyridazinyl and Ar<sup>3</sup> is substituted phenyl.
47. The compound of Claim 46 wherein HetAr is pyridinyl, pyrimidinyl, pyrazinyl, or pyridazinyl and Ar<sup>3</sup> is substituted phenyl.

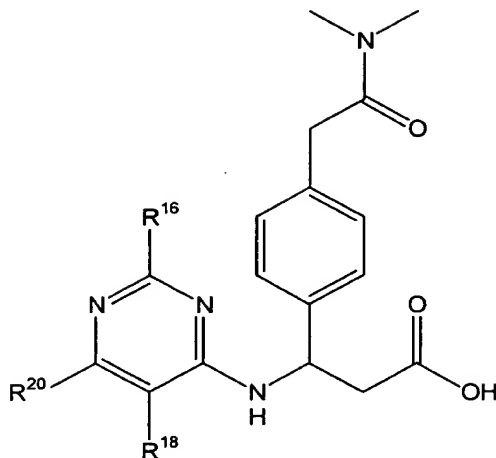
48. A method for treating a disease mediated by VLA-4 in a patient, wherein the disease is selected from the group consisting of asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, acute juvenile onset diabetes, inflammatory bowel disease, ulcerative colitis, Crohn's disease, multiple sclerosis, rheumatoid arthritis, tissue transplantation, tumor metastasis, meningitis, encephalitis, stroke, and other cerebral traumas, nephritis, retinitis, atopic dermatitis, psoriasis, myocardial ischemia, acute leukocyte-mediated lung injury, adult respiratory distress syndrome, erythema nodosum, allergic conjunctivitis, optic neuritis, uveitis, allergic rhinitis, Ankylosing spondylitis, psoriatic arthritis, vasculitis, Reiter's syndrome, systemic lupus erythematosus, progressive systemic sclerosis, polymyositis, dermatomyositis, Wegner's granulomatosis, aortitis, sarcoidosis, lymphocytopenia, temporal arteritis, pericarditis, myocarditis, congestive heart failure, polyarteritis nodosa, hypersensitivity syndromes, allergy, hypereosinophilic syndromes, Churg-Strauss syndrome, chronic obstructive pulmonary disease, hypersensitivity pneumonitis, chronic active hepatitis, interstitial cystitis, autoimmune endocrine failure, primary biliary cirrhosis, autoimmune aplastic anemia, chronic persistent hepatitis and thyroiditis, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of any one of Claims 27-32 or 34-47.
49. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of any one of Claims 27-32 or 34-47.

50. A method for treating a disease mediated by VLA-4 in a patient, wherein the disease is selected from the group consisting of asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, acute juvenile onset diabetes, inflammatory bowel disease, ulcerative colitis, Crohn's disease, multiple sclerosis, rheumatoid arthritis, tissue transplantation, tumor metastasis, meningitis, encephalitis, stroke, and other cerebral traumas, nephritis, retinitis, atopic dermatitis, psoriasis, myocardial ischemia, acute leukocyte-mediated lung injury, adult respiratory distress syndrome, erythema nodosum, allergic conjunctivitis, optic neuritis, uveitis, allergic rhinitis, Ankylosing spondylitis, psoriatic arthritis, vasculitis, Reiter's syndrome, systemic lupus erythematosus, progressive systemic sclerosis, polymyositis, dermatomyositis, Wegner's granulomatosis, aortitis, sarcoidosis, lymphocytopenia, temporal arteritis, pericarditis, myocarditis, congestive heart failure, polyarteritis nodosa, hypersensitivity syndromes, allergy, hypereosinophilic syndromes, Churg-Strauss syndrome, chronic obstructive pulmonary disease, hypersensitivity pneumonitis, chronic active hepatitis, interstitial cystitis, autoimmune endocrine failure, primary biliary cirrhosis, autoimmune aplastic anemia, chronic persistent hepatitis and thyroiditis, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 33.
51. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 33.
52. A method for binding VLA-4 in a biological sample which method comprises contacting the biological sample, comprising blood or plasma withdrawn from

a patient, with a compound of Claim 27 under conditions wherein said compound binds to VLA-4.



53. A compound having the structure



wherein:

R<sup>16</sup> is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

R<sup>18</sup> is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic; and

R<sup>20</sup> is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen.

54. A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 53.
55. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 53.
56. A method for binding VLA-4 in a biological sample which method comprises contacting the biological sample, comprising blood or plasma withdrawn from a patient, with a compound of Claim 53 under conditions wherein said compound binds to VLA-4.